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METHODS OF TREATING AND PREVENTING RSV, HMPV, AND PIV USING ANTI-RSV, ANTI-HMPV, AND ANTI-PIV ANTIBODIES

Abstract:

Abstract of WO2004010935

The present invention relates to methods for broad spectrum prevention and treatment of viral respiratory infections. In particular, the present invention relates to methods for preventing, treating or ameliorating symptoms associated with respiratory syncytial virus (RSV), parainfluenza virus (PIV), and/or human metapneumovirus (hMPV) infection, the methods comprising administering to a subject an effective amount of one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof, and/or one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, a certain serum titer of the anti-RSV-antigen antibodies, andt-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof is achieved in said subject. In certain specific embodiments, the subject is human and, preferably, the anti-RSV-antigen antibody, anti-PIV-antigen antibody, and/or anti-hMPV-antigen antibodies are human or humanized. The present invention relates further to compositions comprising the anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof. The present invention also relates to detectable or diagnostic compositions comprising the one or more anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen binding fragments thereof and methods for detecting or diagnosing RSV, PIV, and/or hMPV infection utilizing the compositions.

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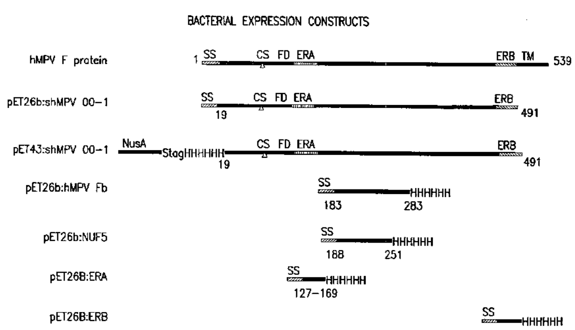

(57) Abstract: The present invention relates to methods for broad spectrum prevention and treatment of viral respiratory infections. In particular, the present invention relates to methods for preventing, treating or ameliorating symptoms associated with respiratory syncytial virus (RSV), parainfluenza virus (PIV), and/or human metapneumovirus (hMPV) infection, the methods comprising administering to a subject an effective amount of one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof, and/or one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, a certain serum titer of the anti-RSV-antigen antibodies, andt-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof is achieved in said subject. In certain specific embodiments, the subject is human and, preferably, the anti-RSV-antigen antibody, anti-PIV-antigen antibody, and/or anti-hMPV-antigen antibodies are human or humanized. The present invention relates further to compositions comprising the anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof. The present invention also relates to detectable or diagnostic compositions comprising the one or more anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen binding fragments thereof and methods for detecting or diagnosing RSV, PIV, and/or hMPV infection utilizing the compositions.

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METHODS OF TREATING AND PREVENTING RSV, HMPV, AND PIV USING ANTI-RSV, ANTI-HMPV, AND ANTI-PIV ANTIBODIES

RELATED APPLICATIONS

This application claims benefit of United States provisional application No.: 60/398,475, filed July 25, 2002, which is incorporated herein by reference in its entirety.

1. INTRODUCTION

The present invention provides methods for broad spectrum prevention and treatment of viral respiratory infection. In particular, the present invention relates to methods for preventing, treating or ameliorating symptoms associated with respiratory syncytial virus (RSV), parainfluenza virus (PIV), and/or human metapneumovirus (hMPV) infection, the methods comprising administering to a subject an effective amount of one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof, and/or one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, a certain serum titer of the anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof is achieved in said subject. In certain specific embodiments, the subject is human and, preferably, the anti-RSV-antigen antibody, anti-PIV-antigen antibody, and/or anti-hMPV-antigen antibodies are human or humanized. The present invention relates further to compositions comprising the anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof. The present invention also relates to detectable or diagnostic compositions comprising the one or more anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof and methods for detecting or diagnosing RSV, PIV and/or hMPV infection utilizing the compositions.

2. BACKGROUND OF THE INVENTION

2.1. PIV INFECTIONS

Parainfluenza viral infection results in serious respiratory tract disease in infants and children. (Tao, *et al.*, 1999, Vaccine 17: 1100-08). Infectious parainfluenza viral infections account for approximately 20% of all hospitalizations of pediatric patients suffering from respiratory tract infections worldwide. *Id.*

PIV is a member of the paramyxovirus genus of the paramyxovirus family. PIV is made up of two structural modules: (1) an internal ribonucleoprotein core, or nucleocapsid, containing the viral genome, and (2) an outer, roughly spherical lipoprotein envelope. Its genome is a single strand of negative sense RNA, approximately 15,456 nucleotides in length, encoding at least eight polypeptides. These proteins include, but are not limited to, the nucleocapsid structural protein (NP, NC, or N depending on the genera), the phospoprotein (P), the matrix protein (M), the fusion glycoprotein (F), the hemagglutinin-neuraminidase glycoprotein (HN), the large polymerase protein (L), and the C and D proteins of unknown function. *Id.*

The parainfluenza nucleocapsid protein (NP, NC, or N) consists of two domains within each protein unit including an amino-terminal domain, comprising about two-thirds of the molecule, which interacts directly with the RNA, and a carboxyl-terminal domain, which lies on the surface of the assembled nucleocapsid. A hinge is thought to exist at the junction of these two domains thereby imparting some flexibility to this protein (see Fields *et al.* (ed.), 1991, Fundamental Virology, Second Edition, Raven Press, New York, incorporated by reference herein in its entirety). The matrix protein (M), is apparently involved with viral assembly and interacts with both the viral membrane as well as the nucleocapsid proteins. The phosphoprotein (P), which is subject to phosphorylation, is thought to play a regulatory role in transcription, and may also be involved in methylation, phosphorylation and polyadenylation. The fusion glycoprotein (F) interacts with the viral membrane and is first produced as an inactive precursor, then cleaved post-translationally to produce two disulfide linked polypeptides. The active F protein is also involved in penetration of the parainfluenza virion into host cells by facilitating fusion of the viral envelope with the host cell plasma membrane. *Id.* The glycoprotein, hemagglutinin-neuraminidase (HN), protrudes from the envelope allowing the virus to contain both hemagglutinin and neuraminidase activities. HN is strongly hydrophobic at its amino terminal which functions to anchor the HN protein into

the lipid bilayer. *Id.* Finally, the large polymerase protein (L) plays an important role in both transcription and replication. *Id.*

2.2 RSV INFECTIONS

Respiratory syncytial virus (RSV) is the leading cause of serious lower respiratory tract disease in infants and children (Feigen et al., eds., 1987, *In: Textbook of Pediatric Infectious Diseases*, WB Saunders, Philadelphia at pages 1653-1675; New Vaccine Development, Establishing Priorities, Vol. 1, 1985, National Academy Press, Washington DC at pages 397-409; and Ruuskanen et al., 1993, Curr. Probl. Pediatr. 23:50-79). The yearly epidemic nature of RSV infection is evident worldwide, but the incidence and severity of RSV disease in a given season vary by region (Hall, C.B., 1993, Contemp. Pediatr. 10:92-110). In temperate regions of the northern hemisphere, it usually begins in late fall and ends in late spring. Primary RSV infection occurs most often in children from 6 weeks to 2 years of age and uncommonly in the first 4 weeks of life during nosocomial epidemics (Hall et al., 1979, New Engl. J. Med. 300:393-396). Children at increased risk from RSV infection include, but are not limited to, preterm infants (Hall et al., 1979, New Engl. J. Med. 300:393-396) and children with bronchopulmonary dysplasia (Groothuis et al., 1988, Pediatrics 82:199-203), congenital heart disease (MacDonald et al., New Engl. J. Med. 307:397-400), congenital or acquired immunodeficiency (Ogra et al., 1988, Pediatr. Infect. Dis. J. 7:246-249; and Pohl et al., 1992, J. Infect. Dis. 165:166-169), and cystic fibrosis (Abman et al., 1988, J. Pediatr. 113:826-830). The fatality rate in infants with heart or lung disease who are hospitalized with RSV infection is 3%-4% (Navas et al., 1992, J. Pediatr. 121:348-354).

RSV infects adults as well as infants and children. In healthy adults, RSV causes predominantly upper respiratory tract disease. It has recently become evident that some adults, especially the elderly, have symptomatic RSV infections more frequently than had been previously reported (Evans, A.S., eds., 1989, Viral Infections of Humans. Epidemiology and Control, 3rd ed., Plenum Medical Book, New York at pages 525-544). Several epidemics also have been reported among nursing home patients and institutionalized young adults (Falsey, A.R., 1991, Infect. Control Hosp. Epidemiol. 12:602608; and Garvie et al., 1980, Br. Med. J. 281:1253-1254). Finally, RSV may cause serious disease in immunosuppressed persons, particularly bone marrow transplant patients (Hertz et al., 1989, Medicine 68:269-281).

Treatment options for established RSV disease are limited. Severe RSV disease of the lower respiratory tract often requires considerable supportive care, including administration of humidified oxygen and respiratory assistance (Fields et al., eds, 1990, Fields Virology, 2nd ed., Vol. 1, Raven Press, New York at pages 1045-1072).

While a vaccine might prevent RSV infection, no vaccine is yet licensed for this indication. A major obstacle to vaccine development is safety. A formalin-inactivated vaccine, though immunogenic, unexpectedly caused a higher and more severe incidence of lower respiratory tract disease due to RSV in immunized infants than in infants immunized with a similarly prepared trivalent parainfluenza vaccine (Kim et al., 1969, Am. J. Epidemiol. 89:422-434; and Kapikian et al., 1969, Am. J. Epidemiol. 89:405-421). Several candidate RSV vaccines have been abandoned and others are under development (Murphy et al., 1994, Virus Res. 32:13-36), but even if safety issues are resolved, vaccine efficacy must also be improved. A number of problems remain to be solved. Immunization would be required in the immediate neonatal period since the peak incidence of lower respiratory tract disease occurs at 2-5 months of age. The immaturity of the neonatal immune response together with high titers of maternally acquired RSV antibody may be expected to reduce vaccine immunogenicity in the neonatal period (Murphy et al., 1988, J. Virol. 62:3907-3910; and Murphy et al., 1991, Vaccine 9:185-189). Finally, primary RSV infection and disease do not protect well against subsequent RSV disease (Henderson et al., 1979, New Engl. J. Med. 300:530-534).

Currently, the only approved approach to prophylaxis of RSV disease is passive immunization. Initial evidence suggesting a protective role for IgG was obtained from observations involving maternal antibody in ferrets (Prince, G.A., Ph.D. diss., University of California, Los Angeles, 1975) and humans (Lambrecht et al, 1976, J. Infect. Dis. 134:211-217; and Glezen et al., 1981, J. Pediatr. 98:708-715). Hemming et al. (Morell et al., eds., 1986, Clinical Use of Intravenous Immunoglobulins, Academic Press, London at pages 285-294) recognized the possible utility of RSV antibody in treatment or prevention of RSV infection during studies involving the pharmacokinetics of an intravenous immune globulin (IVIG) in newborns suspected of having neonatal sepsis. They noted that 1 infant, whose respiratory secretions yielded RSV, recovered rapidly after IVIG infusion. Subsequent analysis of the IVIG lot revealed an unusually high titer of RSV neutralizing antibody. This same group of investigators then examined the ability of hyperimmune serum or immune globulin, enriched for RSV neutralizing antibody, to protect cotton rats and primates against

RSV infection (Prince et al., 1985, Virus Res. 3:193-206; Prince et al., 1990, J. Virol. 64:3091-3092; Hemming et al., 1985, J. Infect. Dis. 152:1083-1087; Prince et al., 1983, Infect. Immun. 42:81-87; and Prince et al., 1985, J. Virol. 55:517-520). Results of these studies suggested that RSV neutralizing antibody given prophylactically inhibited respiratory tract replication of RSV in cotton rats. When given therapeutically, RSV antibody reduced pulmonary viral replication both in cotton rats and in a nonhuman primate model. Furthermore, passive infusion of immune serum or immune globulin did not produce enhanced pulmonary pathology in cotton rats subsequently challenged with RSV.

Recent clinical studies have demonstrated the ability of this passively administered RSV hyperimmune globulin (RSV IVIG) to protect at-risk children from severe lower respiratory infection by RSV (Groothius et al., 1993, New Engl. J. Med. 329:1524-1530; and The PREVENT Study Group, 1997, Pediatrics 99:93-99). While this is a major advance in preventing RSV infection, this treatment poses certain limitations in its widespread use. First, RSV IVIG must be infused intravenously over several hours to achieve an effective dose. Second, the concentrations of active material in hyperimmune globulins are insufficient to treat adults at risk or most children with comprised cardiopulmonary function. Third, intravenous infusion necessitates monthly hospital visits during the RSV season. Finally, it may prove difficult to select sufficient donors to produce a hyperimmune globulin for RSV to meet the demand for this product. Currently, only approximately 8% of normal donors have RSV neutralizing antibody titers high enough to qualify for the production of hyperimmune globulin.

One way to improve the specific activity of the immunoglobulin would be to develop one or more highly potent RSV neutralizing monoclonal antibodies (MAbs). Such MAbs should be human or humanized in order to retain favorable pharmacokinetics and to avoid generating a human anti-mouse antibody response, as repeat dosing would be required throughout the RSV season. Two glycoproteins, F and G, on the surface of RSV have been shown to be targets of neutralizing antibodies (Fields et al., 1990, *supra*; and Murphy et al., 1994 , *supra*). These two proteins are also primarily responsible for viral recognition and entry into target cells; G protein binds to a specific cellular receptor and the F protein promotes fusion of the virus with the cell. The F protein is also expressed on the surface of infected cells and is responsible for subsequent fusion with other cells leading to syncytia formation. Thus, antibodies to the F protein may directly neutralize virus or block entry of the virus into the cell or prevent syncytia formation. Although antigenic and structural

differences between A and B subtypes have been described for both the G and F proteins, the more significant antigenic differences reside on the G glycoprotein, where amino acid sequences are only 53% homologous and antigenic relatedness is 5% (Walsh et al., 1987, J. Infect. Dis. 155:1198-1204; and Johnson et al., 1987, Proc. Natl. Acad. Sci. USA 84:5625-5629). Conversely, antibodies raised to the F protein show a high degree of cross-reactivity among subtype A and B viruses. Beeler and Coelingh (1989, J. Virol. 7:2941-2950) conducted an extensive analysis of 18 different murine MAbs directed to the RSV F protein. Comparison of the biologic and biochemical properties of these MAbs resulted in the identification of three distinct antigenic sites (designated A, B, and C). Neutralization studies were performed against a panel of RSV strains isolated from 1956 to 1985 that demonstrated that epitopes within antigenic sites A and C are highly conserved, while the epitopes of antigenic site B are variable.

A humanized antibody directed to an epitope in the A antigenic site of the F protein of RSV, SYNAGIS®, is approved for intramuscular administration to pediatric patients for prevention of serious lower respiratory tract disease caused by RSV at recommended monthly doses of 15 mg/kg of body weight throughout the RSV season (November through April in the northern hemisphere). SYNAGIS® is a composite of human (95%) and murine (5%) antibody sequences. See, Johnson et al., 1997, J. Infect. Diseases 176:1215-1224 and U.S. Patent No. 5,824,307, the entire contents of which are incorporated herein by reference. The human heavy chain sequence was derived from the constant domains of human IgG_1 and the variable framework regions of the VH genes of Cor (Press et al., 1970, Biochem. J. 117:641-660) and Cess (Takashi et al., 1984, Proc. Natl. Acad. Sci. USA 81:194-198). The human light chain sequence was derived from the constant domain of $C\kappa$ and the variable framework regions of the VL gene K104 with $J\kappa$-4 (Bentley et al., 1980, Nature 288:5194-5198). The murine sequences derived from a murine monoclonal antibody, Mab 1129 (Beeler et al., 1989, J. Virology 63:2941-2950), in a process which involved the grafting of the murine complementarity determining regions into the human antibody frameworks.

2.3 AVIAN AND HUMAN METAPNEUMOVIRUS

Recently, a new member of the *Paramyxoviridae* family has been isolated from 28 children with clinical symptoms reminiscent of those caused by hRSV infection, ranging from mild upper respiratory tract disease to severe bronchiolitis and pneumonia (Van Den Hoogen et al., 2001, Nature Medicine 7:719-724). The new virus was named human

metapneumovirus (hMPV) based on sequence homology and gene constellation. The study further showed that by the age of five years virtually all children in the Netherlands have been exposed to hMPV and that the virus has ben circulating in humans for at least half a century.

The genomic organization of human metapneumovirus is described in van den Hoogen et al, 2002, Virology 295:119-132. Human metapneumovirus has recently been isolated from patients in North America (Peret et al., 2002, J. Infect. Diseases 185:1660-1663).

Human metapneumovirus is related to avian metapneumovirus. For exampe, the F protein of hMPV is highly homologous to the F protein of APV. Alignment of the human metapneumoviral F protein with the F protein of an avian pneumovirus isolated from Mallard Duck shows 85.6% identity in the ectodomain. Alignment of the human metapneumoviral F protein with the F protein of an avian pneumovirus isolated from Turkey (subgroup B) shows 75% identity in the ectodomain. See, *e.g.*, co-owned and co-pending Provisional Application No.: 60/358,934, entitled "Recombinant Parainfluenza Virus Expression Systems and Vaccines Comprising Heterologous Antigens Derived from Metapneumovirus", filed on February 21, 2002, by Haller and Tang, which is incorporated herein by reference in its entirety.

Respiratory disease caused by an avian pneumovirus (APV) was first described in South Africa in the late 1970s (Buys et al., 1980, Turkey 28:36-46) where it had a devastating effect on the turkey industry. The disease in turkeys was characterized by sinusitis and rhinitis and was called turkey rhinotracheitis (TRT). The European isolates of APV have also been strongly implicated as factors in swollen head syndrome (SHS) in chickens (O'Brien, 1985, Vet. Rec. 117:619-620). Originally, the disease appeared in broiler chicken flocks infected with Newcastle disease virus (NDV) and was assumed to be a secondary problem associated with Newcastle disease (ND). Antibody against European APV was detected in affected chickens after the onset of SHS (Cook et al., 1988, Avian Pathol. 17:403-410), thus implicating APV as the cause.

The avian pneumovirus is a single stranded, non-segmented RNA virus that belongs to the sub-family *Pneumovirinae* of the family *Paramyxoviridae,* genus metapneumovirus (Cavanagh and Barrett, 1988, Virus Res. 11:241-256; Ling et al., 1992, J. Gen. Virol. 73:1709-1715; Yu et al., 1992, J. Gen. Virol. 73:1355-1363). The *Paramyxoviridae* family is divided into two sub-families: the *Paramyxovirinae* and *Pneumovirinae*. The subfamily

Paramyxovirinae includes, but is not limited to, the genera: Paramyxovirus, Rubulavirus, and Morbillivirus. Recently, the sub-family *Pneumovirinae* was divided into two genera based on gene order, *i.e. pneumovirus* and *metapneumovirus* (Naylor et al., 1998, J. Gen. Virol., 79:1393-1398; Pringle, 1998, Arch. Virol. 143:1449-1159). The *pneumovirus* genus includes, but is not limited to, human respiratory syncytial virus (HRSV), bovine respiratory syncytial virus (BRSV), ovine respiratory syncytial virus, and mouse pneumovirus. The *metapneumovirus* genus includes, but is not limited to, European avian pneumovirus (subgroups A and B), which is distinguished from HRSV, the type species for the genus *pneumovirus* (Naylor et al., 1998, J. Gen. Virol., 79:1393-1398; Pringle, 1998, Arch. Virol. 143:1449-1159). The US isolate of APV represents a third subgroup (subgroup C) within *metapneumovirus* genus because it has been found to be antigenically and genetically different from European isolates (Seal, 1998, Virus Res. 58:45-52; Senne et al., 1998, In: Proc. 47th WPDC, California, pp. 67-68).

Electron microscopic examination of negatively stained APV reveals pleomorphic, sometimes spherical, virions ranging from 80 to 200 nm in diameter with long filaments ranging from 1000 to 2000 nm in length (Collins and Gough, 1988, J. Gen. Virol. 69:909-916). The envelope is made of a membrane studded with spikes 13 to 15 nm in length. The nucleocapsid is helical, 14 nm in diameter and has 7 nm pitch. The nucleocapsid diameter is smaller than that of the genera Paramyxovirus and Morbillivirus, which usually have diameters of about 18 nm.

Avian pneumovirus infection is an emerging disease in the USA despite its presence elsewhere in the world in poultry for many years. In May 1996, a highly contagious respiratory disease of turkeys appeared in Colorado, and an APV was subsequently isolated at the National Veterinary Services Laboratory (NVSL) in Ames, Iowa (Senne et al., 1997, Proc. 134th Ann. Mtg., AVMA, pp. 190). Prior to this time, the United States and Canada were considered free of avian pneumovirus (Pearson et al., 1993, In: Newly Emerging and Re-emerging Avian Diseases: Applied Research and Practical Applications for Diagnosis and Control, pp. 78-83; Hecker and Myers, 1993, Vet. Rec. 132:172). Early in 1997, the presence of APV was detected serologically in turkeys in Minnesota. By the time the first confirmed diagnosis was made, APV infections had already spread to many farms. The disease is associated with clinical signs in the upper respiratory tract: foamy eyes, nasal discharge and swelling of the sinuses. It is exacerbated by secondary infections. Morbidity

in infected birds can be as high as 100%. The mortality can range from 1 to 90% and is highest in six to twelve week old poults.

Avian pneumovirus is transmitted by contact. Nasal discharge, movement of affected birds, contaminated water, contaminated equipment; contaminated feed trucks and load-out activities can contribute to the transmission of the virus. Recovered turkeys are thought to be carriers. Because the virus is shown to infect the epithelium of the oviduct of laying turkeys and because APV has been detected in young poults, egg transmission is considered a possibility.

Based upon the recent work with hMPV, hMPV likewise appears to be a significant factor in human, particularly, juvenile respiratory disease.

Thus, theses three viruses, RSV, hMPV, and PIV, cause a significant portion of human respiratory disease. What is needed is a broad spectrum prophylaxis to reduce the incidence of viral respiratory disease.

Citation or discussion of a reference herein shall not be construed as an admission that such is prior art to the present invention.

2.4 VIRUS ENTRY INTO HOST CELL

It is emerging that some of the enveloped viruses, *e.g.*, retrovirus, orthomyxovirus, filovirus, and paramyxovirus, might use a fusion mechanism involving so-called heptad repeats to gain entry into a host cell (Eckert et al., 2001, Annu. Rev. Biochem. 70:777-810; Weissenhorn et. al., 1999, Mol. Membr. Biol. 16:3-9; Lamb et. al., 1999, Mol. Membr. Biol. 16:11-19; Skehel et al., 2000, Annu. Rev. Biochem. 69:531-569; Bentz, J., 2000, Biophys J. 78:886-900; Peisajovich et. al., 2002, Trends Biochem. Sci. 27:183-190). According to this model, the fusion peptide located at the N-terminus of the F protein (*e.g.*, of paramyxovirus) is exposed to insert itself into the cell membrane. Further, fusion proteins undergo conformational changes during fusion (Wang et al., 2003, Biochem. Biophys. Res. Comm. 302:469-475). The highly conserved heptad repeat (HR) regions have been implicated in facilitation of the fusion process (Wang et al., 2003, Biochem. Biophys. Res. Comm. 302:469-475). Therefore, the heptad repeats are an attractive target for the prevention of virus infection and/or propagation through the inhibition of fusion with a host cell.

3 SUMMARY OF THE INVENTION

The present invention provides methods for broad spectrum prevention and treatment of viral respiratory infections. Viruses are major causes of severe respiratory infections, particularly in infants, prematurely born infants, the elderly, immunocompromised patients, recipients of transplants, etc. Respiratory infections can be effectively prevented and/or treated using the combination therapies/prophylaxes provided by the present invention. The present invention provides broad spectrum combination therapy/prophylaxis comprising administering to a subject (i) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof; (ii) one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof; and/or (iii) one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. By providing to the subject a plurality of antibodies directed to antigens of a variety of viruses, the risk of respiratory viral infection is reduced in the subject. A particular advantage of administering antibodies of different immunospecificities is that different strains of viruses and viruses with naturally occuring modifications do not escape the immunity of the subject but are recognized by at least one of the plurality of antibodies.

In certain embodiments, the invention provides a method of preventing a viral infection in a subject, said method comprising administering to the subject: (i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and (ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof neutralize RSV. In certain embodiments, the one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof neutralize hMPV. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof block RSV infection of cells of the subject. In certain embodiments, the one or more anti-hMPV-antigen antibodies antibodies or antigen-binding fragments thereof block hMPV infection of cells of the subject.

In certain embodiments, the invention provides a method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject: (i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-

binding fragments thereof bind immunospecifically to a RSV antigen; and (ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or a fragments thereof bind immunospecifically to a RSV antigen; and (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or a fragments thereof bind immunospecifically to a hMPV antigen, wherein the first dose reduces the incidence of RSV infection by at least 25% and wherein the second dose reduces the incidence of hMPV infection by at least 25%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 50% and wherein the second dose reduces the incidence of hMPV infection by at least 50%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 75% and wherein the second dose reduces the incidence of hMPV infection by at least 75%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 90% and wherein the second dose reduces the incidence of hMPV infection by at least 90%.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen, wherein the serum titer of said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and wherein the serum titer of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof.

In certain embodiments, the amino acid sequence of the RSV antigen is that of SEQ ID NO:390 to 398, respectively. In certain embodiments, the amino acid sequence of the

RSV antigen is 90% identical to the amino acid sequence of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, or RSV G protein. In certain embodiments, the the RSV antigen is selected from the group consisting of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, and RSV G protein. In certain embodiments, the one or more anti-RSV-antigen antibodies immunospecifically bind to an antigen of Group A or Group B RSV. In certain embodiments, the RSV antigen is RSV F protein. In certain embodiments, the one or more anti-hMPV-antigen antibodies cross-react with a turkey APV antigen. In certain embodiments, the one or more anti-hMPV-antigen antibodies are (i) human or humanized antibodies and (ii) cross-react with a turkey APV antigen. In certain embodiments, the turkey APV antigen is selected from the group consisting of turkey APV nucleoprotein, turkey APV phosphoprotein, turkey APV matrix protein, turkey APV small hydrophobic protein, turkey APV RNA-dependent RNA polymerase, turkey APV F protein, and turkey APV G protein. In certain embodiments, the turkey APV antigen is an antigen of avian pneumovirus type A, avian pneumovirus type B, or avian pneumovirus type C. In certain embodiments, the amino acid sequence of said turkey APV antigen is that of SEQ ID NO:424 to 429, respectively. In certain embodiments, the amino acid sequence of the hMPV antigen is that of SEQ ID NO:399 to 406, 420, or 421, respectively. In certain embodiments, the hMPV antigen is selected from the group consisting of hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and hMPV G protein. In certain embodiments, the hMPV antigen is hMPV F protein. In certain embodiments, the anti-RSV-antigen antibody is SYNAGIS™ (Palivizumab); AFFF; P12f2 P12f4; P11d4; Ale9; A12a6; A13c4; A17d4; A4B4; 1X-493L1; FR H3-3F4; M3H9; Y10H6; DG; AFFF(1); 6H8; L1-7E5; L2-15B10; A13a11; A1h5; A4B4(1);A4B4-F52S; or A4B4L1FR-S28R. In certain embodiments, the effective amount of said one or more anti-RSV-antigen antibodies is 100 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-RSV-antigen antibodies is 10 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-RSV-antigen antibodies is 1 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof is 100 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof is 10 mg/kg

or less. In certain embodiments, the effective amount of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof is 1 mg/kg or less. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, the one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered concurrently. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations of said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations are separated by a time period from each other. In certain embodiments, the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and/or said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered by a nebulizer or an inhaler. In certain embodiments, the one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and/or said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered intramuscularly, intravenously or subcutaneously. In certain embodiments, the viral infection is an infection with RSV and hMPV. In certain

embodiments, the viral infection is an infection with RSV and APV. In certain embodiments, at least one of said antibodies is a monoclonal antibody, a synthetic antibody, an intrabody, a chimeric antibody, a human antibody, a humanized chimeric antibody, a humanized antibody, a glycosylated antibody, a multispecific antibody, a human antibody, a single-chain antibody, or a bispecific antibody. In certain embodiments, at least one of said antibodies is a human antibody. In certain embodiments, at least one of said antibodies is a humanized antibody. In certain embodiments, at least one of said antibodies is a synthetic antibody. In certain embodiments, the subject is a mammal. In certain embodiments, the mammal is a primate. In certain embodiments, the primate is a human. In certain embodiments, the human is an elderly human. In certain embodiments, the human is a transplant recipient. In certain embodiments, the human is an immunocompromised patient. In certain embodiments, the human is an AIDS patient. In certain embodiments, the human is an infant. In certain embodiments, the human has cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency, or acquired immunodeficiency or has had a bone marrow transplant. In certain embodiments, infant was born prematurely or is at risk of hospitalization for a RSV infection and/or for a hMPV infection. In certain embodiments, the human infant was born prematurely. In certain embodiments, the infant is less than 32 weeks of gestational age. In certain embodiments, the infant is between 32 and 35 weeks of gestational age. In certain embodiments, the infant is more than 35 weeks of gestational age. In certain embodiments, the infant is more than 38 weeks of gestational age. In certain embodiments, the mammal is not a primate. In certain embodiments, the non-primate mammal is an animal model for RSV infection and/or hMPV infection. In certain embodiments, the non-primate mammal is a cotton rat. In certain embodiments, the antibody is administered once a month just prior to and during the RSV season. In certain embodiments, the antibody is administered every two months just prior to and during the RSV season. In certain embodiments, the antibody is administered once just prior to or during the RSV season. In certain embodiments, at least one of said fragments is a Fab fragment, a F(ab') fragment, a $F(ab')_2$ fragment, a Fd, a single-chain Fv, a disulfide-linked Fv, a fragment comprising a V_L domain, or a fragment comprising a V_H domain.

In certain embodiments, the invention provides a method of preventing a viral infection in a subject, said method comprising administering to the subject: (i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein said one or more antibodies

or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen.

In certain embodiments, the invention provides method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject: (i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein said one or more antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein said one or more antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen, wherein the dose reduces the incidence of hMPV infection by at least 25%. In certain embodiments, wherein the dose reduces the incidence of hMPV infection by at least 50%. In certain embodiments, wherein the dose reduces the incidence of hMPV infection by at least 75%. In certain embodiments, wherein the dose reduces the incidence of hMPV infection by at least 90%.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein said one or more antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen, wherein the serum titer of said one or more antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more antibodies or antigen-binding fragments thereof.

In certain embodiments, the invention provides a pharmaceutical composition, said composition comprising: (i) one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and (ii) one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen. In certain embodiments, the amino acid sequence of the RSV antigen is that of SEQ ID NO:390 to 398, respectively. In certain embodiments, the amino acid sequence of the RSV antigen is 90% identical to the amino acid sequence of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV

small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, or RSV G protein. In certain embodiments, the RSV antigen is selected from the group consisting of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, and RSV G protein. In certain embodiments, said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof immunospecifically bind to an antigen of Group A or Group B RSV. In certain embodiments, the RSV antigen is RSV F protein. In certain embodiments, said one or more anti-hMPV-antigen antibodies cross-react with a turkey APV antigen. In certain embodiments, said one or more anti-hMPV-antigen antibodies are (i) human or humanized antibodies and (ii) cross-react with a turkey APV antigen. In certain embodiments, said turkey APV antigen is selected from the group consisting of turkey APV nucleoprotein, turkey APV phosphoprotein, turkey APV matrix protein, turkey APV small hydrophobic protein, turkey APV RNA-dependent RNA polymerase, turkey APV F protein, and turkey APV G protein.In certain embodiments, said turkey APV antigen is an antigen of avian pneumovirus type A, avian pneumovirus type B, or avian pneumovirus type C. In certain embodiments, the amino acid sequence of said turkey APV antigen is that of SEQ ID NO:424 to 429, respectively. In certain embodiments, the amino acid sequence of the hMPV antigen is that of SEQ ID NO:399 to 406, 420, or 421, respectively. In certain embodiments, the hMPV antigen is selected from the group consisting of hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and hMPV G protein. In certain embodiments, the hMPV antigen is hMPV F protein. In certain embodiments, the anti-RSV-antigen antibody is SYNAGIS™; AFFF; P12f2 P12f4; P11d4; Ale9; A12a6; A13c4; A17d4; A4B4; 1X-493L1; FR H3-3F4; M3H9; Y10H6; DG; AFFF(1); 6H8; L1-7E5; L2-15B10; A13a11; A1h5; A4B4(1);A4B4-F52S; or A4B4L1FR-S28R. In certain embodiments, at least one of said antibodies is a monoclonal antibody, a synthetic antibody, an intrabody, a chimeric antibody, a human antibody, a humanized chimeric antibody, a humanized antibody, a glycosylated antibody, a multispecific antibody, a human antibody, a single-chain antibody, or a bispecific antibody. In certain embodiments, at least one of said antibodies is a human antibody. In certain embodiments, at least one of said antibodies is a humanized antibody. In certain embodiments, at least one of said antibodies is a synthetic antibody. In certain embodiments, at least one of said fragments is a Fab fragment, a F(ab') fragment, a $F(ab')_2$

fragment, a Fd, a single-chain Fv, a disulfide-linked Fv, a fragment comprising a V_L domain, or a fragment comprising a V_H domain.

In certain embodiments, the application provides a pharmaceutical composition, said composition comprising: one or more antibodies or antigen-binding fragments thereof, wherein said one or more antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen.

In certain embodiments, the invention provides a method comprising administering to the subject: (i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen; and (ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof neutralize PIV. In certain embodiments, said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof neutralize hMPV. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof block PIV infection of cells of the subject. In certain embodiments, said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof block hMPV infection of cells of the subject.

In certain embodiments, the invention provides a method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject: (i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen; and (ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or a fragments thereof bind immunospecifically to a PIV antigen; and (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more

second antibodies or a fragments thereof bind immunospecifically to a hMPV antigen, wherein the first dose reduces the incidence of PIV infection by at least 25% and wherein the second dose reduces the incidence of hMPV infection by at least 25%. In certain embodiments, the first dose reduces the incidence of PIV infection by at least 50% and wherein the second dose reduces the incidence of hMPV infection by at least 50%. In certain embodiments, the first dose reduces the incidence of PIV infection by at least 75% and wherein the second dose reduces the incidence of hMPV infection by at least 75%. In certain embodiments, the first dose reduces the incidence of PIV infection by at least 90% and wherein the second dose reduces the incidence of hMPV infection by at least 90%.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen; and (ii) a second dose of one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof, wherein said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen, wherein the serum titer of said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and wherein the serum titer of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, the amino acid sequence of the PIV antigen is that of SEQ ID NO:407 to 419, respectively. In certain embodiments, the amino acid sequence of the PIV antigen is 90% identical to the amino acid sequence of PIV nucleocapsid phosphoprotein, PIV L protein, PIV matrix protein, PIV HN glycoprotein, PIV RNA-dependent RNA polymerase, PIV Y1 protein, PIV D protein, or PIV C protein. In certain embodiments, the PIV antigen is selected from the group consisting of PIV nucleocapsid phosphoprotein, PIV L protein, PIV matrix protein, PIV HN glycoprotein, PIV RNA-dependent RNA polymerase, PIV Y1 protein, PIV D protein, or PIV C protein. In certain embodiments, said one or more anti-hMPV-antigen antibodies immunospecifically bind to an antigen of human PIV type 1, human PIV type 2, human PIV type 3, or human PIV type 4. In certain embodiments, the PIV antigen is PIV F protein. In certain embodiments, said one or more anti-hMPV-antigen antibodies cross-react with a turkey APV

antigen. In certain embodiments, said one or more anti-hMPV-antigen antibodies are (i) human or humanized antibodies and (ii) cross-react with a turkey APV antigen. In certain embodiments, said turkey APV antigen is selected from the group consisting of turkey APV nucleoprotein, turkey APV phosphoprotein, turkey APV matrix protein, turkey APV small hydrophobic protein, turkey APV RNA-dependent RNA polymerase, turkey APV F protein, and turkey APV G protein. In certain embodiments, said turkey APV antigen is an antigen of avian pneumovirus type A, avian pneumovirus type B, or avian pneumovirus type C. In certain embodiments, the amino acid sequence of said turkey APV antigen is that of SEQ ID NO:424 to 429, respectively. In certain embodiments, the amino acid sequence of the hMPV antigen is that of SEQ ID NO:399-406, 420, or 421, respectively. In certain embodiments, the hMPV antigen is selected from the group consisting of hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and hMPV G protein. In certain embodiments, the hMPV antigen is hMPV F protein. In certain embodiments, the effective amount of said one or more anti-PIV-antigen antibodies is 100 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-PIV-antigen antibodies is 10 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-PIV-antigen antibodies is 1 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof is 100 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof is 10 mg/kg or less. In certain embodiments, the effective amount of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof is 1 mg/kg or less. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered concurrently. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations of

said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations are separated by a time period from each other. In certain embodiments, the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and/or said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered by a nebulizer or an inhaler. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and/or said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered intramuscularly, intravenously or subcutaneously. In certain embodiments, the viral infection is an infection with PIV and hMPV. In certain embodiments, the viral infection is an infection with PIV and APV. In certain embodiments, at least one of said antibodies is a monoclonal antibody, a synthetic antibody, an intrabody, a chimeric antibody, a human antibody, a humanized chimeric antibody, a humanized antibody, a glycosylated antibody, a multispecific antibody, a human antibody, a single-chain antibody, or a bispecific antibody. In certain embodiments, at least one of said antibodies is a human antibody. In certain embodiments, at least one of said antibodies is a humanized antibody. In certain embodiments, at least one of said antibodies is a synthetic antibody. In certain embodiments, the subject is a mammal. In certain embodiments, the mammal is a primate. In certain embodiments, the primate is a human. In certain embodiments, the human is an elderly human. In certain embodiments, the human is a transplant recipient. In certain embodiments, the human is an immunocompromised patient. In certain embodiments, the human is an AIDS patient. In certain embodiments, the human is an infant. In certain embodiments, the

human has cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency, or acquired immunodeficiency or has had a bone marrow transplant. In certain embodiments, the infant was born prematurely or is at risk of hospitalization for a PIV infection and/or a hMPV infection. In certain embodiments, the infant was born prematurely. In certain embodiments, the infant is less than 32 weeks of gestational age. In certain embodiments, the infant is 32 and 35 weeks of gestational age. In certain embodiments, the infant is 35 weeks of gestational age. In certain embodiments, infant is more than 38 weeks of gestational age. In certain embodiments, the mammal is not a primate. In certain embodiments, the non-primate mammal is an animal model for PIV infection and/or hMPV infection. In certain embodiments, the non-primate mammal is a cotton rat. In certain embodiments, the antibody is administered once a month just prior to and during the PIV season. In certain embodiments, the antibody is administered every two months just prior to and during the PIV season. In certain embodiments, the antibody is administered once just prior to or during the PIV season. In certain embodiments, at least one of said fragments is a Fab fragment, a F(ab') fragment, a F(ab')$_2$ fragment, a Fd, a single-chain Fv, a disulfide-linked Fv, a fragment comprising a V_L domain, or a fragment comprising a V_H domain.

In certain embodiments, the invention provides a method of preventing a viral infection in a subject, said method comprising administering to the subject: (i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; (ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen; and (iii) a prophylactically effective amount of one or more third antibodies or antigen-binding fragments thereof, wherein said one or more third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen. In certain embodiments, said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof neutralize RSV. In certain embodiments, said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof neutralize hMPV. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof neutralize PIV. In certain embodiments, said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof block RSV infection of cells of the subject. In certain embodiments, said one or more anti-hMPV-antigen antibodies or antigen-binding fragments

thereof block hMPV infection of cells of the subject. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof block PIV infection of cells of the subject.

In certain embodiments, the invention provides a method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject: (i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; (ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen; and (iii) a therapeutically effective amount of one or more third antibodies or antigen-binding fragments thereof, wherein said one or more third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or a fragments thereof bind immunospecifically to a RSV antigen; (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or a fragments thereof bind immunospecifically to a hMPV antigen; and (iii) a third dose of one or more third antibodies or antigen-binding fragments thereof, wherein said one or more third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen, wherein the first dose reduces the incidence of RSV infection by at least 25%, wherein the second dose reduces the incidence of hMPV infection by at least 25%, and wherein the third dose reduces the incidence of PIV infection by at least 25%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 50%, the second dose reduces the incidence of hMPV infection by at least 50%, and the third dose reduces the incidence of PIV infection by at least 50%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 75%, the second dose reduces the incidence of hMPV infection by at least 75%, and the third dose reduces the incidence of PIV infection by at least 75%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 90%, the second dose reduces the incidence of hMPV infection by at least 90%, and the third antibody reduces the incidence of PIV infection by at least 90%.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen; and (iii) a third dose of one or more third antibodies or antigen-binding fragments thereof, wherein said one or more third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen, wherein the serum titer of said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, wherein the serum titer of said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof, and wherein the serum titer of said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, the amino acid sequence of the PIV antigen is that of SEQ ID NO:407 to 419, respectively. In certain embodiments, the amino acid sequence of the PIV antigen is 90% identical to the amino acid sequence of PIV nucleoprotein, PIV phosphoprotein, PIV matrix protein, PIV small hydrophobic protein, PIV RNA-dependent RNA polymerase, PIV F protein, or PIV G protein. In certain embodiments, the PIV antigen is selected from the group consisting of PIV nucleoprotein, PIV phosphoprotein, PIV matrix protein, PIV small hydrophobic protein, PIV RNA-dependent RNA polymerase, PIV F protein, and PIV G protein.

In certain embodiments, the invention provides a method of preventing a viral infection in a subject, said method comprising administering to the subject: (i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and (ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen. In certain embodiments, said one or more anti-RSV-antigen antibodies or

antigen-binding fragments thereof neutralize RSV. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof neutralize PIV. In certain embodiments, said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof block RSV infection of cells of the subject. In certain embodiments, said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof block PIV infection of cells of the subject.

In certain embodiments, the invention provides a method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject: (i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and (ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or a fragments thereof bind immunospecifically to a RSV antigen; and (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or a fragments thereof bind immunospecifically to a PIV antigen, wherein the first dose reduces the incidence of RSV infection by at least 25% and wherein the second dose reduces the incidence of PIV infection by at least 25%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 50% and wherein the second dose reduces the incidence of hMPV infection by at least 50%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 75% and wherein the second dose reduces the incidence of hMPV infection by at least 75%. In certain embodiments, the first dose reduces the incidence of RSV infection by at least 90% and wherein the second dose reduces the incidence of hMPV infection by at least 90%.

In certain embodiments, the invention provides a method of passive immunotherapy, said method comprising administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein

said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen, wherein the serum titer of said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and wherein the serum titer of said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof.

3.1. BRIEF DESCRIPTION OF THE FIGURES

Figure 1. Expression constructs for the expression of the hMPV F protein.

3.2. DEFINITIONS

The term "analog" of a certain polypeptide as used herein refers to a polypeptide that possesses a similar or identical function as the certain polypeptide or a fragment of the certain polypeptide, the certain polypeptide can be, *e.g.*, an antibody or an antigen-binding fragment thereof, but does not necessarily comprise a similar or identical amino acid sequence to the certain polypeptide or fragment thereof, or possess a similar or identical structure to the certain polypeptide.

A polypeptide that has a similar amino acid sequence to a certain polypeptide refers to a polypeptide that satisfies at least one of the following: (a) a polypeptide having an amino acid sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or at least 99% identical to the amino acid sequence the certain polypeptide; (b) a polypeptide encoded by a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence encoding the certain polypeptide of at least 5 amino acid residues, at least 10 amino acid residues, at least 15 amino acid residues, at least 20 amino acid residues, at least 25 amino acid residues, at least 40 amino acid residues, at least 50 amino acid residues, at least 60 amino residues, at least 70 amino acid residues, at least 80 amino acid residues, at least 90 amino acid residues, at least 100 amino acid residues, at least 125 amino acid residues, or at least 150 amino acid residues; and (c) a polypeptide encoded by a nucleotide sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least

80%, at least 85%, at least 90%, at least 95% or at least 99% identical to the nucleotide sequence encoding the certain polypeptide. A polypeptide with similar structure to a certain polypeptide refers to a polypeptide that has a similar secondary, tertiary or quaternary structure to a certain polypeptide. The structure of a polypeptide can be determined by methods known to those skilled in the art, including but not limited to, X-ray crystallography, nuclear magnetic resonance, and crystallographic electron microscopy. A certain polypeptide in the context of the present invention can be RSV polypeptide, an APV polypeptide, a hMPV polypeptide, a PIV polypeptide, a fragment of a RSV polypeptide, a fragment of an APV polypeptide, a fragment of a hMPV polypeptide, a fragment of a PIV polypeptide, an antibody that immunospecifically binds to a RSV polypeptide, an antibody that immunospecifically binds to an APV polypeptide, an antibody that immunospecifically binds to a PIV polypeptide, an antibody that immunospecifically binds to a hMPV polypeptide, an antibody fragment that immunospecifically binds to a RSV polypeptide, an antibody fragment that immunospecifically binds to an APV polypeptide, an antibody fragment that immunospecifically binds to a PIV polypeptide, or an antibody fragment that immunospecifically binds to a hMPV polypeptide.

As used herein, the terms "antibody" and "antibodies" refer to monoclonal antibodies, multispecific antibodies (*e.g.*, bi-specific), human antibodies, humanized antibodies, camelised antibodies, chimeric antibodies, single-chain Fvs (scFv), single chain antibodies, synthetic antibodies, single domain antibodies, Fab fragments, F(ab) fragments, disulfide-linked Fvs (sdFv), and anti-idiotypic (anti-Id) antibodies, and epitope-binding fragments of any of the above. In particular, antibodies include immunoglobulin molecules and immunologically active fragments of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site. Immunoglobulin molecules can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA and IgY), class (*e.g.*, IgG_1, IgG_2, IgG_3, IgG_4, IgA_1 and IgA_2) or subclass.

As used herein, the term "in combination" refers to the use of more than one prophylactic and/or therapeutic agents. The use of the term "in combination" does not restrict the order in which prophylactic and/or therapeutic agents are administered to a subject with a respiratory viral infection. A first prophylactic or therapeutic agent can be administered prior to (*e.g.*, 5 minutes, 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours, 96 hours, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 8 weeks, or 12 weeks before), concomitantly with, or subsequent to (*e.g.*, 5 minutes, 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12

hours, 24 hours, 48 hours, 72 hours, 96 hours, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 8 weeks, or 12 weeks after) the administration of a second prophylactic or therapeutic agent to a subject which was or is susceptible to a respiratory viral infection. Any additional prophylactic or therapeutic agent can be administered in any order with the other additional prophylactic or therapeutic agents.

As used herein, the term "synergistic" refers to a combination of prophylactic or therapeutic agents which is more effective than the additive effects of any two or more single agents. A synergistic effect of a combination of prophylactic or therapeutic agents permits the use of lower dosages of one or more of the agents and/or less frequent administration of said agents to a subject with a respiratory viral infection. The ability to utilize lower dosages of prophylactic or therapeutic agents and/or to administer said agents less frequently reduces the toxicity associated with the administration of said agents to a subjectd without reducing the efficacy of said agents in the prevention or treatment of respiratory viral infections. In addition, a synergistic effect can result in improved efficacy of agents in the prevention or treatment of respiratory viral infections. Finally, synergistic effect of a combination of prophylactic or therapeutic agents may avoid or reduce adverse or unwanted side effects associated with the use of any single therapy.

The term "derivative" as used herein refers to a polypeptide that has been altered by the introduction of amino acid residue substitutions, deletions or additions. The term "derivative" refers also to a polypeptide that has been modified, *i.e*, by the covalent attachment of any type of molecule to the polypeptide. Further modifications are, *inter alia*, glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein. Modifications include, *inter alia*, chemical modifications by techniques known to those of skill in the art, *e.g.*, chemical cleavage, acetylation, formylation, synthesis in the presence of tunicamycin, etc. Further, a derivative if a certain polypeptide can be generated by introducing one or more non-classical amino acids into the certain polypeptide. A polypeptide derivative possesses a similar or identical function as the certain polypeptide from which it is derived.

The term "effective neutralizing titer" as used herein refers to the amount of antibody which corresponds to the amount present in the serum of animals (human or cotton rat) that has been shown to be either clinically efficacious (in humans) or to reduce virus by 99% in,

for example, cotton rats. The 99% reduction is defined by a specific challenge of, *e.g.*, 10^3 pfu, 10^4 pfu, 10^5 pfu, 10^6 pfu, 10^7 pfu, 10^8 pfu, or 10^9 pfu of RSV, PIV, and/or hMPV.

The term "epitopes" as used herein refers to a portion of a protein or polypeptide having antigenic and/or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. An epitope having immunogenic activity is a portion of a protein or polypeptide that elicits an antibody response in an animal. An epitope having antigenic activity is a portion of a protein or polypeptide to which an antibody immunospecifically binds as determined by any method well known in the art, for example, by the immunoassays described herein. Antigenic epitopes need not necessarily be immunogenic.

The term "fragment" as used herein refers to a peptide or polypeptide comprising an amino acid sequence of at least 5 contiguous amino acid residues, at least 10 contiguous amino acid residues, at least 15 contiguous amino acid residues, at least 20 contiguous amino acid residues, at least 25 contiguous amino acid residues, at least 40 contiguous amino acid residues, at least 50 contiguous amino acid residues, at least 60 contiguous amino residues, at least 70 contiguous amino acid residues, at least contiguous 80 amino acid residues, at least contiguous 90 amino acid residues, at least contiguous 100 amino acid residues, at least contiguous 125 amino acid residues, at least 150 contiguous amino acid residues, at least contiguous 175 amino acid residues, at least contiguous 200 amino acid residues, or at least contiguous 250 amino acid residues of the amino acid sequence of a polypeptide, protein, or antibody. Preferably, a fragment has the reactive activity of the polypeptide, protein, or antibody.

The term "human infant" as used herein refers to a human less than 24 months, preferably less than 16 months, less than 12 months, less than 6 months, less than 3 months, less than 2 months, or less than 1 month of age. In certain embodiments, the human infant is born at more than 38 weeks of gestational age.

The term "human infant born prematurely" as used herein refers to a human born at less than 40 weeks gestational age, less than 35 weeks gestational age. In specific embodiments, the prematurely born human infant is of between 30-35 weeks of gestational age. In specific embodiments, the prematurely born human infant is of between 35-38 weeks of gestational age. In certain embodiments, the prematurely born infant is of 38 weeks gestational age, preferably, the infant is of less than 38 weeks gestational age.

An "isolated" or "purified" antibody or fragment thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the

protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of an antibody or antibody fragment in which the antibody or antibody fragment is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, an antibody or antibody fragment that is substantially free of cellular material includes preparations of antibody or antibody fragment having less than about 30%, 20%, 10%, or 5% (by dry weight) of heterologous protein (also referred to herein as a "contaminating protein"). When the antibody or antibody fragment is recombinantly produced, it is also preferably substantially free of culture medium, *i.e.*, culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When the antibody or antibody fragment is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, *i.e.*, it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of the antibody or antibody fragment have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the antibody or antibody fragment of interest. In a preferred embodiment, antibodies of the invention or fragments thereof are isolated or purified.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. In a preferred embodiment, nucleic acid molecules encoding antibodies of the invention or fragments thereof are isolated or purified.

The term "fusion protein" as used herein refers to a polypeptide that comprises an amino acid sequence of an antibody or fragment thereof and an amino acid sequence of a heterologous polypeptide (*e.g.*, a non-anti-RSV antibody, a non-anti-PIV antibody, a non-anti-APV antibody and/or a non-anti-hMPV antibody).

The term "high potency" as used herein refers to antibodies or antigen-binding fragments thereof that exhibit high potency as determined in various assays for biological activity (*e.g.*, neutralization of RSV, APV, hMPV, PIV) such as those described herein. For example, high potency antibodies of the present invention or fragments thereof have an EC_{50} value less than 0.01 nM, less than 0.025 nM, less than 0.05 nM, less than 0.1 nM, less than

0.25 nM, less than 0.5 nM, less than 0.75 nM, less than 1 nM, less than 1.25 nM, less than 1.5 nM, less than 1.75 nM, or less than 2 nM as measured by a microneutralization assay described herein. Further, high potency antibodies of the present invention or fragments thereof result in at least a 30%, 40%, 50%, 60%, 75%, preferably at least a 95% and more preferably a 99% lower RSV titer, PIV titer, APV titer, and/or hMPV titer in a subject, such as a cotton rat 5 days after challenge with 10^5 pfu relative to a subject, such as a cotton rat, not administered with said antibodies or antibody fragments. In certain embodiments of the invention, high potency antibodies of the present invention or fragments thereof exhibit a high affinity and/or high avidity for one or more RSV antigens, one or more PIV antigens, one or more hMPV antigens, and/or one or more APV antigens (*e.g.*, antibodies or antibody fragments having an affinity of at least $2X10^8$ M^{-1}, at least $2.5X10^8$ M^{-1}, at least $5X10^8$ M^{-1}, at least 10^9 M^{-1}, at least 5 X 10^9 M^{-1}, at least 10^{10} M^{-1}, at least 5 X 10^{10} M^{-1}, at least 10^{11} M^{-1}, at least 5 X 10^{11} M^{-1}, at least 10^{12} M^{-1}, or at least 5 X 10^{12} M^{-1} for one or more RSV antigens, one or more PIV antigens, one or more hMPV antigens, and/or one or more APV antigens).

The term "host" as used herein refers to a mammal, preferably a human.

The term "host cell" as used herein refers to the particular subject cell transfected with a nucleic acid molecule and the progeny or potential progeny of such a cell. Progeny of such a cell may not be identical to the parent cell transfected with the nucleic acid molecule due to mutations or environmental influences that may occur in succeeding generations or integration of the nucleic acid molecule into the host cell genome.

In certain embodiments of the invention, a "prophylactically effective serum titer" is the serum titer in a mammal, preferably a human, that reduces the incidence of a respiratory viral infection, particularly a RSV infection, a hMPV infection, a PIV infection, and/or a APV infection in a subject. Preferably, the prophylactically effective serum titer reduces the incidence of RSV infections, hMPV infections, PIV infections, and/or APV infections in a subject with the greatest probability of complications resulting from RSV infection, hMPV infection, PIV infection, and/or APV infection, respectively (*e.g.*, a subject with cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency or acquired immunodeficiency, a subject who has had a bone marrow transplant, a human infant, or an elderly human). In certain other embodiments of the invention, a "prophylactically effective serum titer" is the serum titer in a cotton rat that results in a RSV titer, hMPV titer, PIV titer, and/or APV titer 5 days after challenge with 10^5 pfu that is 90%, *i.e.*, 1 log, lower than the RSV titer, hMPV titer, PIV titer, and/or APV titer 5 days after

challenge with 10^5 pfu of RSV, hMPV, APV, and/or PIV, respectively, in a cotton rat not administered an antibody or antibody fragment that immunospecifically binds to a RSV antigen, hMPV antigen, PIV antigen, and/or APV antigen, respectively. A prophylactically effective amount includes an amount that is prophylactically effective in combination with other agents, even if it is not prophylactically effective by itself.

In certain embodiments of the invention, a "therapeutically effective serum titer" is the serum titer in a mammal, preferably a human, that reduces the severity, the duration and/or the symptoms associated with a respiratory viral infection, particularly with a RSV infection, a hMPV infection, an APV infection, and/or a PIV infection in said mammal. Preferably, the therapeutically effective serum titer reduces the severity, the duration and/or the number symptoms associated with RSV infections, hMPV infections, APV infections, and/or PIV infections in humans with the greatest probability of complications resulting from a RSV, APV, hMPV, and/or PIV infection (*e.g.*, a human with cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency or acquired immunodeficiency, a human who has had a bone marrow transplant, a human infant, or an elderly human). In certain other embodiments of the invention, a "therapeutically effective serum titer" is the serum titer in a cotton rat that results in a RSV, APV, hMPV, and/or PIV titer 5 days after challenge with 10^5 pfu that is 90%, *i.e.*, 1 log, lower than the RSV, APV, hMPV, and/or PIV titer 5 days after challenge with 10^5 pfu of RSV APV, hMPV, and/or PIV, respectively, in a cotton rat not administered an antibody or antibody fragment that immunospecifically binds to a RSV, APV, hMPV, and/or PIV antigen, respectively. A therapeutically effective amount includes an amount that is therapeutically effective in combination with other agents, even if it is not therapeutically effective by itself.

The term "anti-PIV-antigen antibody" refers to an antibody or antibody fragment thereof that binds immunospecifically to a PIV antigen. A PIV antigen refers to a PIV polypeptide or fragment thereof such as of PIV nucleocapsid structural protein, PIV phosphoprotein, PIV fusion glycoprotein, PIV L protein, PIV matrix protein, PIV HN glycoprotein, PIV RNA-dependent RNA polymerase, PIV Y1 protein, PIV D protein, or PIV C protein. A PIV antigen also refers to a polypeptide that has a similar amino acid sequence compared to a PIV nucleocapsid structural protein, PIV phosphoprotein, PIV fusion glycoprotein, PIV L protein, PIV matrix protein, PIV HN glycoprotein, PIV RNA-dependent RNA polymerase, PIV Y1 protein, PIV D protein, or PIV C protein.

The term "anti-RSV-antigen antibody" refers to an antibody or antibody fragment thereof that binds immunospecifically to a RSV antigen. A RSV antigen refers to a RSV polypeptide or fragment thereof such as of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RSV polymerase, RSV F protein, and RSV G protein. A RSV antigen also refers to a polypeptide that has a similar amino acid sequence compared to a RSV polypeptide or fragment thereof such as of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RSV polymerase, RSV F protein, and RSV G protein.

The term "anti-hMPV-antigen antibody" refers to an antibody or antibody fragment thereof that binds immunospecifically to a hMPV antigen. A hMPV antigen refers to a hMPV polypeptide or fragment thereof such as of hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent hMPV polymerase, hMPV F protein, and hMPV G protein. A hMPV antigen also refers to a polypeptide that has a similar amino acid sequence compared to a hMPV polypeptide or fragment thereof such as of hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent hMPV polymerase, hMPV F protein, and hMPV G protein.

The term "serum titer" as used herein refers to an average serum titer in a population of least 10, preferably at least 20, and most preferably at least 40 subjects.

The term "subject" as used herein refers to vertebrate, preferably to a mammal. A subject can be a primate, a rat, a mouse, or a cotton rat. Most preferably, the subject is a human.

As used herein, the terms "immunospecifically binds" and "anti-RSV, anti-hMPV, or anti-PIV antibodies" and analogous terms refer to antibodies or fragments thereof that specifically bind to a RSV antigen, a hMPV antigen, or a PIV antigen in an ELISA assay or any other immuno-assay well-known to the skilled artisan (*e.g.*, as described in section 4.8, *infra*). In certain embodiments, an antibody or fragment thereof that immunospecifically binds to a RSV antigen, a hMPV antigen, or a PIV antigen may bind to other peptides or polypeptides with lower or equal affinity as determined by, *e.g.*, immunoassays, BIAcore, or other assays known in the art. In certain other embodiments, an antibody or fragment thereof that immunospecifically binds to a RSV antigen, a hMPV antigen, or a PIV antigen does not bind to other peptides or polypeptides as determined by, *e.g.*, immunoassays, BIAcore, or other assays known in the art. Antibodies or fragments that immunospecifically bind to a

RSV antigen, a hMPV antigen, or a PIV antigen may be cross-reactive with related antigens. Preferably, antibodies or fragments that immunospecifically bind to a RSV antigen, a hMPV antigen, or a PIV antigen do not cross-react with other antigens. Antibodies or fragments that immunospecifically bind to a RSV antigen, a hMPV antigen, or a PIV antigen can be identified, for example, by immunoassays, BIAcore, or other techniques known to those of skill in the art. In certain embodiments, an antibody or fragment thereof binds specifically to a RSV antigen, a hMPV antigen, or a PIV antigen when it binds to a RSV antigen, a hMPV antigen, or a PIV antigen with higher affinity than to any cross-reactive antigen as determined using experimental techniques, such as, but not limited to, radioimmunoassays (RIA), enzyme-linked immunosorbent assays (ELISAs), BIAcore, or other techniques known to those of skill in the art. See, *e.g.*, Paul, ed., 1989, Fundamental Immunology Second Edition, Raven Press, New York at pages 332-336 for a discussion regarding antibody specificity. In certain embodiments, an antibody or fragment thereof binds specifically to a RSV antigen, a hMPV antigen, or a PIV antigen with equal affinity as to any cross-reactive antigen as determined using experimental techniques, such as radioimmunoassays (RIA) and enzyme-linked immunosorbent assays (ELISAs).

To determine the percent identity of two amino acid sequences or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino acid or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (*i.e.*, % identity = number of identical overlapping positions/total number of positions x 100%). In one embodiment, the two sequences are the same length.

The determination of percent identity between two sequences can also be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2264-2268, modified as in Karlin and Altschul, 1993, Proc. Natl. Acad. Sci. U.S.A. 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul et al., 1990, J. Mol. Biol.

215:403. BLAST nucleotide searches can be performed with the NBLAST nucleotide program parameters set, *e.g.*, for score=100, wordlength=12 to obtain nucleotide sequences homologous to a nucleic acid molecules of the present invention. BLAST protein searches can be performed with the XBLAST program parameters set, *e.g.*, to score-50, wordlength=3 to obtain amino acid sequences homologous to a protein molecule of the present invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., 1997, Nucleic Acids Res. 25:3389-3402. Alternatively, PSI-BLAST can be used to perform an iterated search which detects distant relationships between molecules (*Id.*). When utilizing BLAST, Gapped BLAST, and PSI-Blast programs, the default parameters of the respective programs (*e.g.*, of XBLAST and NBLAST) can be used (see, *e.g.*, http://www.ncbi.nlm.nih.gov). Another preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, 1988, CABIOS 4:11-17. Such an algorithm is incorporated in the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, typically only exact matches are counted.

References to RSV, PIV, hMPV, and APV include all groups, subgroups, isolates, types and strains of the respective virus. In a specific embodiment, RSV, PIV, and hMPV refer to all groups, subgroups, isolates, types and strains of human RSV, PIV, and hMPV, respectively.

ABBREVIATIONS

cDNA	complementary DNA
L	large protein
M	matrix protein (lines inside of envelope)
F	fusion glycoprotein
HN	hemagglutinin-neuraminidase glycoprotein
N, NP or NC	nucleoprotein (associated with RNA and required for polymerase activity)
P	phosphoprotein
MOI	multiplicity of infection

NA	neuraminidase (envelope glycoprotein)
PIV	parainfluenza virus
nt	nucleotide
hMPV	human metapneumovirus
APV	avian pneumovirus

4. DETAILED DESCRIPTION OF THE INVENTION

4.1 ANTIBODIES

The invention provides methods of passive immunotherapy for broad-spectrum prevention and, in certain embodiments, treatment of viral respiratory infection. The antibodies to be used with the methods of the invention include antibodies or antigen-binding fragments thereof that bind immunospecifically to a RSV antigen, antibodies or antigen-binding fragments thereof that bind immunospecifically to a hMPV antigen, antibodies or antigen-binding fragments thereof that bind immunospecifically to a PIV antigen, and, in a specific embodiment, human or humanized antibodies that bind immunospecifically to a hMPV antigen and that cross-react with an APV antigen. In a specific embodiment, the antibody to be used with the methods of the invention is an antibody that binds immunospecifically to a hMPV antigen and that cross-reacts with a turkey APV antigen. In a specific embodiment, the antibody to be used with the methods of the invention is a human or humanized antibody that binds immunospecifically to a hMPV antigen and that cross-reacts with a turkey APV antigen. In other specific embodiments, the anti-hMPV antibody does not react with a turkey APV antigen or an APV antigen from any other species of APV.

In certain embodiments, fragments of viral antigens are used as immunogen to produce antibodies to be used with the methods of the invention. In certain embodiments, fragments preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 75 or at least 100 amino acids. In certain, more specific embodiments, a fragment is about 15 to about 30 amino acids long. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof.

In certain embodiments, the anti-PIV-antigen antibody, the anti-RSV-antigen antibody, and/or the anti-hMPV-antigen antibody inhibit the binding of a virus that causes respiratory infection to a cell. In certain embodiments, the anti-PIV-antigen antibody, the anti-RSV-antigen antibody, and/or the anti-hMPV-antigen antibody inhibit in a subject the binding of a virus that causes respiratory infection to a cell of the subject. In certain embodiments, the anti-PIV-antigen antibody, the anti-RSV-antigen antibody, and/or the anti-hMPV-antigen antibody inhibit the infection of a subject with a virus that causes respiratory infections. In certain embodiments, the anti-PIV-antigen antibody, the anti-RSV-antigen antibody, and/or the anti-hMPV-antigen antibody cause neutralization of the virus that causes respiratory infections.

The antibodies to be used with the methods of the invention bind immunospecifically to a variety of viral antigens as discussed in sections 4.1.5, 4.1.6, and 4.1.7 below. In certain embodiments, at least one antibody to be used with the methods of the invention binds immunospecifically to an epitope of an antigen of PIV, hMPV, or RSV, and cross-reacts with another epitope on the same antigen of PIV, hMPV, or RSV, respectively. In certain embodiments, at least one antibody to be used with the methods of the invention binds immunospecifically to an epitope of an antigen of PIV, hMPV, or RSV, and cross-reacts with the analogous antigen of a different virus. For example, an antibody that binds immunospecifically to the F protein of RSV cross reacts with the F protein of hMPV. In a specific embodiment, the anti-RSV-antigen antibody is SYNAGIS®. SYNAGIS® is also known as Palivizumab. The amino acid sequence of SYNAGIS® (Palivizumab) is disclosed in International Application Publication WO 02/43660, entitled "Methods of Administering/Dosing Anti-RSV Antibodies for Prophylaxis and Treatment", by Young et al., which is incorporated herein by reference in its entirety. In another specific embodiment, the anti-RSV-antigen antibody is not SYNAGIS®. In certain specific embodiments, the anti-RSV-antigen antibody is AFFF; P12f2 P12f4; P11d4; Ale9; A12a6; A13c4; A17d4; A4B4; 1X-493L1; FR H3-3F4; M3H9; Y10H6; DG; AFFF(1); 6H8; L1-7E5; L2-15B10; A13a11; A1h5; A4B4(1);A4B4-F52S; or A4B4L1FR-S28R. These antibodies are disclosed in International Application Publication No.: WO 02/43660, entitled "Methods of Administering/Dosing Anti-RSV Antibodies for Prophylaxis and Treatment", by Young et al., which is incorporated herein by reference in its entirety.

In certain embodiments, at least one antibody to be used with the methods of the invention binds immunospecifically to an antigen of one subgroup (type, subtype, group,

isolate etc.) of PIV, hMPV, or RSV and to the analogous antigen of another subgroup (type, subtype, group, isolate etc.) of PIV, hMPV, or RSV, respectively (see sections 4.1.5, 4.1.6, and 4.1.7, respectively).

Antibodies of the invention include, but are not limited to, monoclonal antibodies, multispecific antibodies, synthetic antibodies, human antibodies, humanized antibodies, chimeric antibodies, single-chain Fvs (scFv), single chain antibodies, Fab fragments, F(ab') fragments, disulfide-linked Fvs (sdFv), and anti-idiotypic (anti-Id) antibodies (including, *e.g.*, anti-Id antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. In particular, antibodies of the present invention include immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that immunospecifically binds to a RSV, PIV, APV, and/or hMPV antigen. The immunoglobulin molecules of the invention can be of any type (*e.g.*, IgG, IgE, IgM, IgD, IgA and IgY), class (*e.g.*, IgG_1, IgG_2, IgG_3, IgG_4, IgA_1 and IgA_2) or subclass of immunoglobulin molecule.

The antibodies of the invention may be from any animal origin including birds and mammals (*e.g.*, human, murine, donkey, sheep, rabbit, goat, guinea pig, camel, horse, or chicken). Preferably, the antibodies of the invention are human or humanized monoclonal antibodies. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries (including, but not limited to, synthetic libraries of immunoglobulin sequences homologous to human immunoglobulin sequences) or from mice that express antibodies from human genes.

The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of one antigen of RSV, PIV, or hMPV. In certain embodiments, multispecific antibodies are specific for more than one antigen of RSV, PIV, or hMPV. In certain embodiments, multispecific antibodies are specific for an antigen of RSV and an antigen of hMPV. In certain embodiments, multispecific antibodies are specific for an antigen of PIV and an antigen of hMPV. In certain embodiments, multispecific antibodies are specific for an antigen of PIV and an antigen of RSV. In certain embodiments, multispecific antibodies are specific for an antigen of RSV, an antigen of PIV, and an antigen of hMPV. For multispecific antibodies see, *e.g.*, PCT publications WO 93/17715, WO 92/08802, WO 91/00360, and WO 92/05793; Tutt, et al., J. Immunol. 147:60-69(1991); U.S. Patent Nos.

4,474,893, 4,714,681, 4,925,648, 5,573,920, and 5,601,819; and Kostelny et al., J. Immunol. 148:1547-1553 (1992).

In certain embodiments, high potency antibodies can be used in the methods of the invention. For example, high potency antibodies can be produced by genetically engineering appropriate antibody gene sequences and expressing the antibody sequences in a suitable host. The antibodies produced can be screened to identify antibodies with, *e.g.*, high k_{on} values in a BIAcore assay (see section 4.8.3).

In certain embodiments, an antibody to be used with the methods of the present invention or fragment thereof has an affinity constant or K_a (k_{on}/k_{off}) of at least 10^2 M^{-1}, at least 5 X 10^2 M^{-1}, at least 10^3 M^{-1}, at least 5 X 10^3 M^{-1}, at least 10^4 M^{-1}, at least 5 X 10^4 M^{-1}, at least 10^5 M^{-1}, at least 5 X 10^5 M^{-1}, at least 10^6 M^{-1}, at least 5 X 10^6 M^{-1}, at least 10^7 M^{-1}, at least 5 X 10^7 M^{-1}, at least 10^8 M^{-1}, at least 5 X 10^8 M^{-1}, at least 10^9 M^{-1}, at least 5 X 10^9 M^{-1}, at least 10^{10} M^{-1}, at least 5 X 10^{10} M^{-1}, at least 10^{11} M^{-1}, at least 5 X 10^{11} M^{-1}, at least 10^{12} M^{-1}, at least 5 X 10^{12} M^{-1}, at least 10^{13} M^{-1}, at least 5 X 10^{13} M^{-1}, at least 10^{14} M^{-1}, at least 5 X 10^{14} M^{-1}, at least 10^{15} M^{-1}, or at least 5 X 10^{15} M^{-1}. In yet another embodiment, an antibody to be used with the methods of the invention or fragment thereof has a dissociation constant or K_d (k_{off}/k_{on}) of less than 10^{-2} M, less than 5 X 10^{-2} M, less than 10^{-3} M, less than 5 X 10^{-3} M, less than 10^{-4} M, less than 5 X 10^{-4} M, less than 10^{-5} M, less than 5 X 10^{-5} M, less than 10^{-6} M, less than 5 X 10^{-6} M, less than 10^{-7} M, less than 5 X 10^{-7} M, less than 10^{-8} M, less than 5 X 10^{-8} M, less than 10^{-9} M, less than 5 X 10^{-9} M, less than 10^{-10} M, less than 5 X 10^{-10} M, less than 10^{-11} M, less than 5 X 10^{-11} M, less than 10^{-12} M, less than 5 X 10^{-12} M, less than 10^{-13} M, less than 5 X 10^{-13} M, less than 10^{-14} M, less than 5 X 10^{-14} M, less than 10^{-15} M, or less than 5 X 10^{-15} M.

In certain embodiments, an antibody to be used with the methods of the invention or fragment thereof that has a median effective concentration (EC_{50}) of less than 0.01 nM, less than 0.025 nM, less than 0.05 nM, less than 0.1 nM, less than 0.25 nM, less than 0.5 nM, less than 0.75 nM, less than 1 nM, less than 1.25 nM, less than 1.5 nM, less than 1.75 nM, or less than 2 nM, in an *in vitro* microneutralization assay. The median effective concentration is the concentration of antibody or antibody fragments that neutralizes 50% of the RSV in an *in vitro* microneutralization assay. In a preferred embodiment, an antibody to be used with the methods of the invention or fragment thereof has an EC_{50} of less than 0.01 nM, less than 0.025 nM, less than 0.05 nM, less than 0.1 nM, less than 0.25 nM, less than 0.5 nM, less

than 0.75 nM, less than 1 nM, less than 1.25 nM, less than 1.5 nM, less than 1.75 nM, or less than 2 nM, in an *in vitro* microneutralization assay.

In certain embodiments, the antibodies to be used with the methods of the invention are derivatives of anti-RSV antigen, anti-PIV antigen, and/or anti-hMPV antigen antibodies. Standard techniques known to those of skill in the art can be used to introduce mutations in the nucleotide sequence encoding an antibody to be used with the methods of the invention, including, for example, site-directed mutagenesis and PCR-mediated mutagenesis which result in amino acid substitutions. Preferably, the derivatives include less than 25 amino acid substitutions, less than 20 amino acid substitutions, less than 15 amino acid substitutions, less than 10 amino acid substitutions, less than 5 amino acid substitutions, less than 4 amino acid substitutions, less than 3 amino acid substitutions, or less than 2 amino acid substitutions relative to the original molecule. In a preferred embodiment, the derivatives have conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a side chain with a similar charge. Families of amino acid residues having side chains with similar charges have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Alternatively, mutations can be introduced randomly along all or part of the coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed and the activity of the protein can be determined.

The antibodies to be used with the methods of the invention include derivatives that are modified, *i.e*, by the covalent attachment of any type of molecule to the antibody such that covalent attachment. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, *e.g.*, by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific

chemical cleavage, acetylation, formylation, synthesis in the presence of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

The present invention also provides antibodies of the invention or fragments thereof that comprise a framework region known to those of skill in the art. In certain embodiments, one or more framework regions, preferably, all of the framework regions, of an antibody to be used in the methods of the invention or fragment thereof are human. In certain other embodiments of the invention, the fragment region of an antibody of the invention or fragment thereof is humanized. In certain embodiments, the antibody to be used with the methods of the invention is a synthetic antibody, a monoclonal antibody, an intrabody, a chimeric antibody, a human antibody, a humanized chimeric antibody, a humanized antibody, a glycosylated antibody, a multispecific antibody, a human antibody, a single-chain antibody, or a bispecific antibody.

In certain embodiments of the invention, the antibodies to be used with the invention have half-lives in a mammal, preferably a human, of greater than 12 hours, greater than 1 day, greater than 3 days, greater than 6 days, greater than 10 days, greater than 15 days, greater than 20 days, greater than 25 days, greater than 30 days, greater than 35 days, greater than 40 days, greater than 45 days, greater than 2 months, greater than 3 months, greater than 4 months, or greater than 5 months. Antibodies or antigen-binding fragments thereof having increased *in vivo* half-lives can be generated by techniques known to those of skill in the art. For example, antibodies or antigen-binding fragments thereof with increased *in vivo* half-lives can be generated by modifying (*e.g.*, substituting, deleting or adding) amino acid residues identified as involved in the interaction between the Fc domain and the FcRn receptor (see, *e.g.*, PCT Publication No. WO 97/34631 and U.S. Patent Application No.: 10/020,354, entitled "Molecules with Extended Half-Lives, Compositions and Uses Thereof", filed December 12, 2001, by Johnson et al., which are incorporated herein by reference in their entireties). Such antibodies or antigen-binding fragments thereof can be tested for binding activity to RSV antigens as well as for *in vivo* efficacy using methods known to those skilled in the art, for example, by immunoassays described herein.

Further, antibodies or antigen-binding fragments thereof with increased *in vivo* half-lives can be generated by attaching to said antibodies or antibody fragments polymer molecules such as high molecular weight polyethyleneglycol (PEG). PEG can be attached to said antibodies or antibody fragments with or without a multifunctional linker either through site-specific conjugation of the PEG to the N– or C- terminus of said antibodies or antibody

fragments or via epsilon-amino groups present on lysine residues. Linear or branched polymer derivatization that results in minimal loss of biological activity will be used. The degree of conjugation will be closely monitored by SDS-PAGE and mass spectrometry to ensure proper conjugation of PEG molecules to the antibodies. Unreacted PEG can be separated from antibody-PEG conjugates by, *e.g.*, size exclusion or ion-exchange chromatography. PEG-derivatizated antibodies or antigen-binding fragments thereof can be tested for binding activity to RSV antigens as well as for *in vivo* efficacy using methods known to those skilled in the art, for example, by immunoassays described herein.

In certain embodiments, the antibodies to be used with the methods of the invention are fusion proteins comprising an antibody or fragment thereof that immunospecifically binds to a RSV, PIV, and/or hMPV antigen and a heterologous polypeptide. Preferably, the heterologous polypeptide that the antibody or antibody fragment is fused to is useful for targeting the antibody to respiratory epithelial cells.

In certain embodiments, antibodies to be used with the methods of the invention or fragments thereof disrupt or prevent the interaction between a RSV antigen, a PIV antigen, and/or a hMPV antigen and its host cell receptor.

In certain embodiments, antibodies to be used with the methods of the invention are single-chain antibodies. The design and construction of a single-chain antibody is described in Marasco et al, 1993, Proc Natl Acad Sci 90:7889-7893, which is incorporated herein by reference in its entirety.

In certain embodiments, the antibodies to be used with the invention binds to an intracellular epitope, *i.e.*, are intrabodies. An intrabody comprises at least a portion of an antibody that is capable of immunospecifically binding an antigen and preferably does not contain sequences coding for its secretion. Such antibodies will bind its antigen intracellularly. In one embodiment, the intrabody comprises a single-chain Fv ("sFv"). sFv are antibody fragments comprising the V_H and V_L domains of antibody, wherein these domains are present in a single polypeptide chain. Generally, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv see Pluckthun in *The Pharmacology of Monoclonal Antibodies*, vol. 113, Rosenburg and Moore eds. Springer-Verlag, New York, pp. 269-315 (1994). In a further embodiment, the intrabody preferably does not encode an operable secretory sequence and thus remains within the cell (see

generally Marasco, WA, 1998, "Intrabodies: Basic Research and Clinical Gene Therapy Applications" Springer:New York).

Generation of intrabodies is well-known to the skilled artisan and is described for example in U.S. Patent Nos. 6,004,940; 6,072,036; 5,965,371, which are incorporated by reference in their entireties herein. Further, the construction of intrabodies is discussed in Ohage and Steipe, 1999, J. Mol. Biol. 291:1119-1128; Ohage et al., 1999, J. Mol. Biol. 291:1129-1134; and Wirtz and Steipe, 1999, Protein Science 8:2245-2250, which references are incorporated herein by reference in their entireties. Recombinant molecular biological techniques such as those described for recombinant production of antibodies (*e.g.*, Section 4.1.2 and 4.1.3) may also be used in the generation of intrabodies. A discussion of intrabodies as antiviral agents can also be found in Marasco, 2001, Curr. Top. Microbiol. Immunol. 260:247-270, which is incorporated by reference herein in its entirety.

In particular, the invention provides methods for treating, preventing, and/or ameliorating one or more symptoms of a respiratory infection by administering either: (i) one or more anti-RSV-antigen intrabodies or fragments thereof and one or more anti-PIV-antigen intrabodies or fragments thereof; (ii) one or more anti-PIV-antigen intrabodies or fragments thereof and one or more anti-hMPV-antigen intrabodies or fragments thereof; or (iii) one or more anti-RSV-antigen intrabodies or fragments thereof, one or more anti-PIV-antigen intrabodies or fragments thereof, and one or more anti-hMPV-antigen intrabodies or fragments thereof. The invention also encompasses administering combinations of intrabodies and antibodies or antigen-binding fragments thereof. For example, but not by way of limitation, a method of the invention comprises administering one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and one or more anti-hMPV-antigen intrabodies or fragments thereof.

In one embodiment, intrabodies of the invention retain at least about 75% of the binding effectiveness of the complete antibody *(i.e.*, having constant as well as variable regions) to the antigen. More preferably, the intrabody retains at least 85% of the binding effectiveness of the complete antibody. Still more preferably, the intrabody retains at least 90% of the binding effectiveness of the complete antibody. Even more preferably, the intrabody retains at least 95% of the binding effectiveness of the complete antibody.

In producing intrabodies, polynucleotides encoding variable region for both the V_H and V_L chains of interest can be cloned by using, for example, hybridoma mRNA or splenic mRNA as a template for PCR amplification of such domains (Huse et al., 1989, *Science*

246:1276). In one preferred embodiment, the polynucleotides encoding the V_H and V_L domains are joined by a polynucleotide sequence encoding a linker to make a single chain antibody (sFv). The sFv typically comprises a single peptide with the sequence V_H -linker-V_L or V_L-linker-V_H. The linker is chosen to permit the heavy chain and light chain to bind together in their proper conformational orientation (see for example, Huston, et al., 1991, *Methods in Enzym.* 203:46-121, which is incorporated herein by reference). In a further embodiment, the linker can span the distance between its points of fusion to each of the variable domains (*e.g.*, 3.5 nm) to minimize distortion of the native Fv conformation. In such an embodiment, the linker is a polypeptide of at least 5 amino acid residues, at least 10 amino acid residues, at least 15 amino acid residues, or greater. In a further embodiment, the linker should not cause a steric interference with the V_H and V_L domains of the combining site. In such an embodiment, the linker is 35 amino acids or less, 30 amino acids or less, or 25 amino acids or less. Thus, in a most preferred embodiment, the linker is between 15-25 amino acid residues in length. In a further embodiment, the linker is hydrophilic and sufficiently flexible such that the V_H and V_L domains can adopt the conformation necessary to detect antigen. Intrabodies can be generated with different linker sequences inserted between identical V_H and V_L domains. A linker with the appropriate properties for a particular pair of V_H and V_L domains can be determined empirically by assess the degree of antigen binding for each. Examples of linkers include, but are not limited to, those sequences disclosed in Table 1.

Table 1

Sequence
(Gly Gly Gly Gly Ser)$_3$
Glu Ser Gly Arg Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
Glu Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Ser Thr
Glu Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Ser Thr Gln
Glu Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Val Asp
Gly Ser Thr Ser Gly Ser Gly Lys Ser Ser Glu Gly Lys Gly
Lys Glu Ser Gly Ser Val Ser Ser Glu Gln Leu Ala Gln Phe Arg Ser Leu Asp
Glu Ser Gly Ser Val Ser Ser Glu Glu Leu Ala Phe Arg Ser Leu Asp

In one embodiment, intrabodies are expressed in the cytoplasm. In other embodiments, the intrabodies are localized to various intracellular locations. In such

embodiments, specific localization sequences can be atached to the intranucleotide polypepetide to direct the intrabody to a specific location. Intrabodies can be localized, for example, to the folowing intracellular locations: endoplasmic reticulum (Munro et al., 1987, *Cell* 48:899-907; Hangejorden et al., 1991, *J. Biol. Chem.* 266:6015); nucleus (Lanford et al., 1986, *Cell* 46:575; Stanton et al.,1986, *PNAS* 83:1772; Harlow et al., 1985, *Mol. Cell Biol.* 5:1605); nucleolar region (Seomi et al., 1990, *J. Virology* 64:1803; Kubota et al., 1989, *Biochem. Biophys. Res. Comm.* 162:963; Siomi et al., 1998, *Cell* 55:197); endosomal compartment (Bakke et al., 1990, *Cell* 63:707-716); mitochondrial matrix (Pugsley, A. P., 1989, "Protein Targeting", Academic Press, Inc.); Golgi apparatus (Tang et al., 1992, *J. Bio. Chem.* 267:10122-6); liposomes (Letourneur et al., 1992, *Cell* 69:1183); and plasma membrane (Marchildon et al., 1984, *PNAS* 81:7679-82; Henderson et al., 1987, *PNAS* 89:339-43; Rhee et al., 1987, *J. Virol.* 61:1045-53; Schultz et al., 1984, *J. Virol.* 133:431-7; Ootsuyama et al., 1985, *Jpn. J. Can. Res.* 76:1132-5; Ratner et al., 1985, *Nature* 313:277-84). Examples of localization signals include, but are not limited to, those sequences disclosed in Table 2.

Table 2

Localization	**Sequence**
endoplasmic reticulum	Lys Asp Glu Leu
endoplasmic reticulum	Asp Asp Glu Leu
endoplasmic reticulum	Asp Glu Glu Leu
endoplasmic reticulum	Gln Glu Asp Leu
endoplasmic reticulum	Arg Asp Glu Leu
nucleus	Pro Lys Lys Lys Arg Lys Val
nucleus	Pro Gln Lys Lys Ile Lys Ser
nucleus	Gln Pro Lys Lys Pro
nucleus	Arg Lys Lys Arg
nucleolar region	Arg Lys Lys Arg Arg Gln Arg Arg Arg Ala His Gln
nucleolar region	Arg Gln Ala Arg Arg Asn Arg Arg Arg Arg Trp Arg Glu Arg Gln Arg
nucleolar region	Met Pro Leu Thr Arg Arg Arg Pro Ala Ala Ser Gln Ala Leu Ala Pro Pro Thr Pro
endosomal compartment	Met Asp Asp Gln Arg Asp Leu Ile Ser

Localization	Sequence
	Asn Asn Glu Gln Leu Pro
mitochondrial matrix	Met Leu Phe Asn Leu Arg Xaa Xaa Leu Asn Asn Ala Ala Phe Arg His Gly His Asn Phe Met Val Arg Asn Phe Arg Cys Gly Gln Pro Leu Xaa
plasma membrane	GCVCSSNP
plasma membrane	GQTVTTPL
plasma membrane	GQELSQHE
plasma membrane	GNSPSYNP
plasma membrane	GVSGSKGQ
plasma membrane	GQTITTPL
plasma membrane	GQTLTTPL
plasma membrane	GQIFSRSA
plasma membrane	GQIHGLSP
plasma membrane	GARASVLS
plasma membrane	GCTLSAEE

V_H and V_L domains are made up of the immunoglobulin domains that generally have a conserved structural disulfide bond. In embodiments where the intrabodies are expressed in a reducing environment (*e.g.*, the cytoplasm), such a structural feature cannot exist. Mutations can be made to the intrabody polypeptide sequence to compensate for the decreased stability of the immunoglobulin structure resulting from the absence of disulfide bond formation. In one embodiment, the V_H and/or V_L domains of the intrabodies contain one or more point mutations such that their expression is stabilized in reducing environments (see Steipe et al., 1994, *J. Mol. Biol.* 240:188-92; Wirtz and Steipe, 1999, *Protein Science* 8:2245-50; Ohage and Steipe, 1999, *J. Mol. Biol.* 291:1119-28; Ohage et al., 1999, *J. Mol Biol.* 291:1129-34).

4.1.1 METHODS FOR PRODUCING ANTIBODIES

The antibodies to be used with the methods of the invention or fragments thereof can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

Polyclonal antibodies to a RSV, PIV, and/or hMPV antigen can be produced by various procedures well known in the art. For example, a RSV, PIV, and/or hMPV antigen can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the RSV, PIV, and/or hMPV antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow *et al.*, *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, *et al.*, in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art. Briefly, mice can be immunized with a RSV, PIV, and/or hMPV antigen and once an immune response is detected, *e.g.,* antibodies specific for the RSV, PIV, and/or hMPV antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

In a specific embodiment, an antigen of APV is used to generate antibodies agains hMPV.

In certain embodiments, a method of generating monoclonal antibodies comprises culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with a RSV, PIV, and/or hMPV antigen with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a RSV, PIV, and/or hMPV antigen.

Antibody fragments which recognize specific RSV, PIV, and/or hMPV epitopes may be generated by any technique known to those of skill in the art. For example, Fab and F(ab')2 fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). F(ab')2 fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain. Further, the antibodies to be used with the present invention can also be generated using various phage display methods known in the art.

In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In particular, DNA sequences encoding VH and VL domains are amplified from animal cDNA libraries (*e.g.*, human or murine cDNA libraries of lymphoid tissues). The DNA encoding the VH and VL domains are recombined together with an scFv linker by PCR and cloned into a phagemid vector (*e.g.*, p CANTAB 6 or pComb 3 HSS). The vector is electroporated in *E. coli* and the *E. coli* is infected with helper phage. Phage used in these methods are typically filamentous phage including fd and M13 and the VH and VL domains are usually recombinantly fused to either the phage gene III or gene VIII. Phage expressing an antigen binding domain that binds to a RSV, PIV, and/or hMPV antigen of interest can be selected or identified with antigen, *e.g.*, using labeled antigen or antigen bound or captured to a solid surface or bead. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., 1995, J. Immunol. Methods 182:41-50; Ames et al., 1995, J. Immunol. Methods 184:177-186; Kettleborough et al., 1994, Eur. J. Immunol. 24:952-958; Persic et al., 1997, Gene 187:9-18; Burton et al., 1994, Advances in Immunology 57:191-280; PCT application No. PCT/GB91/O1 134; PCT publication Nos. WO 90/02809, WO 91/10737, WO 92/01047, WO 92/18619, WO 93/1 1236, WO 95/15982,

WO 95/20401, and WO97/13844; and U.S. Patent Nos. 5,698,426, 5,223,409, 5,403,484, 5,580,717, 5,427,908, 5,750,753, 5,821,047, 5,571,698, 5,427,908, 5,516,637, 5,780,225, 5,658,727, 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, *e.g.*, as described below. Techniques to recombinantly produce Fab, Fab' and F(ab')2 fragments can also be employed using methods known in the art such as those disclosed in PCT publication No. WO 92/22324; Mullinax et al., 1992, BioTechniques 12(6):864-869; Sawai et al., 1995, AJRI 34:26-34; and Better et al., 1988, Science 240:1041-1043 (said references incorporated by reference in their entireties).

To generate whole antibodies, PCR primers including VH or VL nucleotide sequences, a restriction site, and a flanking sequence to protect the restriction site can be used to amplify the VH or VL sequences in scFv clones. Utilizing cloning techniques known to those of skill in the art, the PCR amplified VH domains can be cloned into vectors expressing a VH constant region, *e.g.*, the human gamma 4 constant region, and the PCR amplified VL domains can be cloned into vectors expressing a VL constant region, *e.g.*, human kappa or lamba constant regions. Preferably, the vectors for expressing the VH or VL domains comprise an EF-1α promoter, a secretion signal, a cloning site for the variable domain, constant domains, and a selection marker such as neomycin. The VH and VL domains may also cloned into one vector expressing the necessary constant regions. The heavy chain conversion vectors and light chain conversion vectors are then co-transfected into cell lines to generate stable or transient cell lines that express full-length antibodies, *e.g.*, IgG, using techniques known to those of skill in the art.

For some uses, including *in vivo* use of antibodies in humans and *in vitro* detection assays, it may be preferable to use human or chimeric antibodies. Completely human antibodies are particularly desirable for therapeutic treatment of human subjects. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences or synthetic sequences homologous to human immunoglobulin sequences. See also U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO

98/50433, WO 98/24893, WO98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then be bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, *e.g.*, all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, *see, e.g.*, PCT publication Nos. WO 98/24893, WO 96/34096, and WO 96/33735; and U.S. Patent Nos. 5,413,923, 5,625,126, 5,633,425, 5,569,825, 5,661,016, 5,545,806, 5,814,318, and 5,939,598, which are incorporated by reference herein in their entireties. In addition, companies such as Medarex, Inc. (Princeton, NJ), Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

A chimeric antibody is a molecule in which different portions of the antibody are derived from different immunoglobulin molecules such as antibodies having a variable region derived from a non-human (*e.g.*, murine) antibody and a human immunoglobulin constant

region. Methods for producing chimeric antibodies are known in the art. See *e.g.*, Morrison, 1985, Science 229:1202; Oi et al., 1986, BioTechniques 4:214; Gillies et al., 1989, J. Immunol. Methods 125:191-202; and U.S. Patent Nos. 5,807,715, 4,816,567, and 4,816,397, which are incorporated herein by reference in their entireties. Chimeric antibodies comprising one or more CDRs from human species and framework regions from a non-human immunoglobulin molecule can be produced using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication No. WO 91/09967; and U.S. Patent Nos. 5,225,539, 5,530,101, and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, 1991, Molecular Immunology 28(4/5):489-498; Studnicka et al., 1994, Protein Engineering 7(6):805-814; and Roguska et al., 1994, PNAS 91:969-973), and chain shuffling (U.S. Patent No. 5,565,332). In a preferred embodiment, antibodies comprise one or more CDRs listed in Table 3 (preferably all CDRs) and human framework regions. Often, framework residues in the framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, *e.g.*, by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, *e.g.*, Queen et al., U.S. Patent No. 5,585,089; and Riechmann et al., 1988, Nature 332:323, which are incorporated herein by reference in their entireties.)

Further, the antibodies to be used with the methods of the invention can, in turn, be utilized to generate anti-idiotype antibodies that "mimic" RSV, PIV, and/or hMPV antigens using techniques well known to those skilled in the art. (See, *e.g.*, Greenspan & Bona, 1989, FASEB J. 7(5):437-444; and Nissinoff, 1991, J. Immunol. 147(8):2429-2438). For example, antibodies of the invention which bind to and competitively inhibit the binding of RSV, PIV, and/or hMPV (as determined by assays well known in the art) to its host cell receptor can be used to generate anti-idiotypes that "mimic" a RSV, PIV, and/or hMPV antigen and bind to the RSV, PIV, and/or hMPV receptors, *i.e.*, compete with the virus for binding to the host cell, therefore decreasing the infection rate of host cells with virus.

In certain other embodiments, anti-anti-idiotypes, generated by techniques well-known to the skilled artisan, are used in the methods of the invention. Such anti-anti-idiotypes mimic the binding domain of the anti-RSV, -PIV, and/or -hMPV antibody and, as a consequence, bind to and neutralize RSV, PIV, and/or hMPV. Such neutralizing anti-anti-

idiotypes or Fab fragments of such anti-anti-idiotypes can be used in therapeutic regimens to neutralize RSV, PIV, and/or hMPV. For example, such anti-anti-idiotypic antibodies can be used to bind RSV, PIV, and/or hMPV and thereby prevent infection.

In certain embodiments, a fragment of a protein of RSV, PIV, or hMPV is used as an immunogen for the generation of antibodies to be used with the methods of the invention. A fragment of a protein of RSV, PIV, or hMPV to be used as an immunogen can be at least 10, 20, 30, 40, 50, 75, 100, 250, 500, 750, or at least 1000 amino acids in length. In certain embodiments a synthetic peptide of a protein of RSV, PIV, or hMPV is used as an immunogen.

In certain embodiments, fragments of viral antigens are used as immunogen to produce antibodies to be used with the methods of the invention. In certain embodiments, fragments preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 75 or at least 100 amino acids. In certain, more specific embodiments, a fragment is about 15 to about 30 amino acids long. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof.

4.1.2 POLYNUCLEOTIDES ENCODING AN ANTIBODY

Polynucleotides encoding antibodies to be used with the invention may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. Since amino acid sequences of some antibodies are known (as described in Table 2), nucleotide sequences encoding these antibodies can be determined using methods well known in the art, *i.e.*, nucleotide codons known to encode particular amino acids are assembled in such a way to generate a nucleic acid that encodes the antibody or fragment thereof of the invention. Such a polynucleotide encoding the antibody may be assembled from chemically synthesized oligonucleotides (*e.g.*, as described in Kutmeier et al., 1994, BioTechniques 17:242), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (*e.g.*, an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, *e.g.*, a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, *e.g.*, recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel *et al.*, eds., 1998, Current Protocols in Molecular Biology, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

In a specific embodiment, one or more of the CDRs is inserted within framework regions using routine recombinant DNA techniques. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, *e.g.*, Chothia et al., 1998, J. Mol. Biol. 278: 457-479 for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds to a RSV, PIV, and/or hMPV antigen. In certain embodiments, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or

more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

4.1.3 RECOMBINANT EXPRESSION OF AN ANTIBODY

Recombinant expression of an antibody to be used with the methods of the invention, derivative or analog thereof, (*e.g.*, a heavy or light chain of an antibody of the invention or a portion thereof or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably, but not necessarily, containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, a heavy or light chain of an antibody, a heavy or light chain variable domain of an antibody or a portion thereof, or a heavy or light chain CDR, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy, the entire light chain, or both the entire heavy and light chains.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention or fragments thereof, or a heavy or light chain thereof, or portion thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention (see, *e.g.*, U.S. Patent No. 5,807,715). Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention *in situ*. These include but are not limited to microorganisms such as bacteria (*e.g.*, *E. coli* and *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (*e.g.*, *Saccharomyces Pichia*) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (*e.g.*, baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (*e.g.*, Ti plasmid) containing antibody coding sequences; or mammalian cell systems (*e.g.*, COS, CHO, BHK, 293, NS0, and 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (*e.g.*, metallothionein promoter) or from mammalian viruses (*e.g.*, the adenovirus late promoter; the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as *Escherichia coli*, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., 1986, Gene 45:101; and Cockett et al., 1990, Bio/Technology 8:2). In a specific embodiment, the expression of nucleotide sequences encoding antibodies or antigen-binding fragments thereof which immunospecifically bind to one or more RSV antigens is regulated by a constitutive promoter, inducible promoter or tissue specific promoter.

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited to, the *E. coli* expression vector pUR278 (Ruther et al., 1983,

EMBO 12:1791), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, 1985, Nucleic Acids Res. 13:3101-3109; Van Heeke & Schuster, 1989, J. Biol. Chem. 24:5503-5509); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione 5-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The antibody coding sequence may be cloned individually into non-essential regions (for example, the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example, the polyhedrin promoter).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, *e.g.*, the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by *in vitro* or *in vivo* recombination. Insertion in a non-essential region of the viral genome (*e.g.*, region El or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts (*e.g.*, see Logan & Shenk, 1984, Proc. Natl. Acad. Sci. USA 81:355-359). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see, *e.g.*, Bittner et al., 1987, Methods in Enzymol. 153:516-544).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (*e.g.*, glycosylation) and processing (*e.g.*, cleavage) of protein products may be important for the function of the protein. Different host cells have

characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, W138, BT483, Hs578T, HTB2, BT2O and T47D, NS0 (a murine myeloma cell line that does not endogenously produce any immunoglobulin chains), CRL7O3O and HsS78Bst cells.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (*e.g.*, promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compositions that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to, the herpes simplex virus thymidine kinase (Wigler et al., 1977, Cell 11:223), hypoxanthineguanine phosphoribosyltransferase (Szybalska & Szybalski, 1992, Proc. Natl. Acad. Sci. USA 48:202), and adenine phosphoribosyltransferase (Lowy et al., 1980, Cell 22:8-17) genes can be employed in tk-, hgprt- or aprt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: *dhfr*, which confers resistance to methotrexate (Wigler et al., 1980, Natl. Acad. Sci. USA 77:357; O'Hare et al., 1981, Proc. Natl. Acad. Sci. USA 78:1527); *gpt*, which confers resistance to mycophenolic acid (Mulligan & Berg, 1981, Proc. Natl. Acad. Sci. USA 78:2072); neo, which confers resistance to the aminoglycoside G-418 (Wu and Wu, 1991, Biotherapy 3:87-95; Tolstoshev, 1993, Ann. Rev. Pharmacol. Toxicol. 32:573-596; Mulligan, 1993, Science 260:926-932; and

Morgan and Anderson, 1993, Ann. Rev. Biochem. 62: 191-217; May, 1993, TIB TECH 11(5):155-2 15); and *hygro*, which confers resistance to hygromycin (Santerre et al., 1984, Gene 30:147). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel *et al.* (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli *et al.* (eds), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin et al., 1981, J. Mol. Biol. 150:1, which are incorporated by reference herein in their entireties.

The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., 1983, Mol. Cell. Biol. 3:257).

The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, 1986, Nature 322:52; and Kohler, 1980, Proc. Natl. Acad. Sci. USA 77:2 197). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

Once an antibody molecule to be used with the methods of the invention has been produced by recombinant expression, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (*e.g.*, ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation, differential solubility, or by any other standard technique for the purification of proteins. Further, the antibodies of the present invention or

fragments thereof may be fused to heterologous polypeptide sequences described herein or otherwise known in the art to facilitate purification.

4.1.4 BiTE TECHNOLOGY

In certain embodiments, antibodies to be used with the methods of the invention and antibodies of the pharmaceutical compositions of the invention are bispecific T cell engagers (BiTEs). Bispecific T cell engagers (BiTE) are bispecific antibodies that can redirect T cells for antigen-specific elimination of targets. A BiTE molecule has an antigen-binding domain that binds to a T cell antigen (*e.g.* CD3) at one end of the molecule and an antigen binding domain that will bind to an antigen on the target cell. A BiTE molecule was recently described in WO 99/54440, which is herein incorporated by reference. This publication describes a novel single-chain multifunctional polypeptide that comprises binding sites for the CD19 and CD3 antigens (CD19xCD3). This molecule was derived from two antibodies, one that binds to CD19 on the B cell and an antibody that binds to CD3 on the T cells. The variable regions of these different antibodies are linked by a polypeptide sequence, thus creating a single molecule. Also described, is the linking of the variable heavy chain (VH) and light chain (VL) of a specific binding domain with a flexible linker to create a single chain, bispecific antibody.

In an embodiment of this invention, an antibody or a fragment thereof that immunospecifically binds a polypeptide of interest (*e.g.*, an antigen of MPV, RSV and/or PIV) will comprise a portion of the BiTE molecule. For example, the VH and/or VL (preferably a scFV) of an antibody that binds a polypeptide of interest (*e.g.*, an antigen of MPV, RSV and/or PIV) can be fused to an anti-CD3 binding portion such as that of the molecule described above, thus creating a BiTE molecule that targets the polypeptide of interest (*e.g.*, an antigen of MPV, RSV and/or PIV). In addition to the variable heavy and or light chain of antibody against a polypeptide of interest (*e.g.*, an antigen of MPV, RSV and/or PIV), other molecules that bind the polypeptide of interest (*e.g.*, an antigen of MPV, RSV and/or PIV) can comprise the BiTE molecule, for example antiviral compounds. In another embodiment, the BiTE molecule can comprise a molecule that binds to other T cell antigens (other than CD3). For example, ligands and/or antibodies that immunospecifically bind to T-cell antigens like CD2, CD4, CD8, CD11a, TCR, and CD28 are contemplated to be part of this invention. This list is not meant to be exhaustive but only to illustrate that other molecules that can immunospecifically bind to a T cell antigen can be used as part of a BiTE

molecule. These molecules can include the VH and/or VL portions of the antibody or natural ligands (for example LFA3 whose natural ligand is CD3). A BiTE molecule can be an antagonist.

The "binding domain" as used in accordance with the present invention denotes a domain comprising a three-dimensional structure capable of specifically binding to an epitope like native antibodies, free scFv fragments or one of their corresponding immunoglobulin chains, preferably the VH chain. Thus, said domain can comprise the VH and/or VL domain of an antibody or an immunoglobulin chain, preferably at least the VH domain or more preferably the VH and VL domain linked by a flexible polypeptide linker (scFv). On the other hand, said binding domain contained in the polypeptide of interest may comprise at least one complementarity determining region (CDR) of an antibody or immunoglobulin chain recognizing an antigen on the T cell or a cellular antigen. In this respect, it is noted that the binding domain present in the polypeptide of interest may not only be derived from antibodies but also from other T cell or cellular antigen binding protein, such as naturally occurring surface receptors or ligands. It is further contemplated that in an embodiment of the invention, said first and or second domain of the above-described polypeptide mimic or correspond to a VH and VL region from a natural antibody. The antibody providing the binding site for the polypeptide of interest can be, *e.g.*, a monoclonal antibody, polyclonal antibody, chimeric antibody, humanized antibody, bispecific antibody, synthetic antibody, antibody fragment, such as Fab, Fv or scFv fragments etc., or a chemically modified derivative of any of these.

4.1.5 ANTIBODY CONJUGATES

In certain embodiments, the antibodies to be used with the methods of the invention or fragments thereof are recombinantly fused or chemically conjugated (including both covalently and non-covalently conjugations) to a heterologous polypeptide (or portion thereof, preferably at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90 or at least 100 amino acids of the polypeptide) to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. For example, antibodies may be used to target heterologous polypeptides to particular cell types (*e.g.*, respiratory epithelial cells), either *in vitro* or *in vivo*, by fusing or conjugating the antibodies to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to heterologous polypeptides may also be used in *in vitro*

immunoassays and purification methods using methods known in the art. See *e.g.*, PCT publication WO 93/21232; EP 439,095; Naramura *et al.*, Immunol. Lett. 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., PNAS 89:1428-1432 (1992); and Fell et al., J. Immunol. 146:2446-2452(1991), which are incorporated by reference in their entireties.

In certain embodiments, the anti-RSV-antigen antibody is an antibody conjugate. In other embodiments, the anti-PIV-antigen antibody is an antibody conjugate. In other embodiments, the anti-hMPV-antigen antibody is an antibody conjugate.

Additional fusion proteins of the antibodies to be used with the methods of the invention or fragments thereof may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to alter the activities of antibodies of the invention or fragments thereof (*e.g.*, antibodies or antigen-binding fragments thereof with higher affinities and lower dissociation rates). See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308- 13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, antibodies or antigen-binding fragments thereof, or the encoded antibodies or antigen-binding fragments thereof, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more portions of a polynucleotide encoding an antibody or antibody fragment, which portions immunospecifically bind to a RSV, PIV, and/or hMPV antigen may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

Moreover, the antibodies to be used with the methods of the present invention or fragments thereof can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., 1989, Proc. Natl. Acad. Sci. USA 86:821-824, for instance, hexa-histidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the hemagglutinin"HA" tag, which

corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., 1984, Cell 37:767) and the "flag" tag.

An antibody or fragment thereof may be conjugated to a therapeutic moiety such as, but not limited to, a cytotoxin, *e.g.*, a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, *e.g.*, alpha-emitters. A cytotoxin or cytotoxic agent includes, but is not limited to, any agent that is detrimental to cells. Examples include, but are not limited to, paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (*e.g.*, methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating agents (*e.g.*, mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis-dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (*e.g.*, daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (*e.g.*, dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), anti-mitotic agents (*e.g.*, vincristine and vinblastine), and antivirals, such as, but not limited to: nucleoside analogs, such as zidovudine, acyclovir, gangcyclovir, vidarabine, idoxuridine, trifluridine, and ribavirin, as well as foscarnet, amantadine, rimantadine, saquinavir, indinavir, ritonavir, and the alpha-interferons.

Further, an antibody to be used with the methods of the invention or fragment thereof may be conjugated to a therapeutic agent or drug moiety that modifies a given biological response. Therapeutic agents or drug moieties are not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, but are not limited to, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, α-interferon, β-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, *e.g.*, TNF-α, TNF-β, AIM I (see, International Publication No. WO 97/33899), AIM II (see, International Publication No. WO 97/34911), Fas Ligand (Takahashi et al., 1994, J. Iminunol., 6:1567-1574), and VEGI (see, International Publication No. WO 99/23105), a thrombotic agent or an anti-angiogenic agent, *e.g.*, angiostatin or endostatin; or, a biological response modifier such as, for example, a

lymphokine (*e.g.*, interleukin-1 ("IL- 1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), and granulocyte colony stimulating factor ("G-CSF")), or a growth factor (*e.g.*, growth hormone ("GH")).

Techniques for conjugating such therapeutic moieties to antibodies are well known, see, *e.g.*, Arnon *et al.*, "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld *et al.* (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 *(1985);* "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., 1982, Immunol. Rev. 62:119-58.

An antibody or fragment thereof, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

4.1.6 ANTI-RSV-ANTIGEN ANTIBODIES

Anti-RSV-antigen antibodies that can be used with the methods of the invention bind immunospecifically to an antigen of RSV. In certain embodiments, the anti-RSV-antigen antibody binds immunospecifically to an RSV antigen of the Group A of RSV. In certain embodiments, the anti-RSV-antigen antibody binds immunospecifically to an RSV antigen of the Group B of RSV. In certain embodiments, an antibody binds to an antigen of RSV of one Group and cross reacts with the analogous antigen of the other Group.

In certain embodiments, an anti-RSV-antigen antibody binds immunospecifically to a RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, and/or RSV G protein.

In certain embodiments, an anti-RSV-antigen antibody binds to allelic variants of a RSV nucleoprotein, a RSV phosphoprotein, a RSV matrix protein, a RSV small hydrophobic protein, a RSV RNA-dependent RNA polymerase, a RSV F protein, and/or a RSV G protein.

In certain embodiments, the anti-RSV-antigen antibody binds immunospecifically to, *inter alia*, an RSV attachment glycoprotein, *e.g.*, having an amino acid sequence of SEQ ID NO:390; a RSV fusion glycoprotein, *e.g.*, having an amino acid sequence of SEQ ID NO:391; a RSV small hydrophobic protein, *e.g.*, having an amino acid sequence of SEQ ID NO:392; a RSV RNA polymerase beta subunit (Large structural protein) (L protein), *e.g.*, having an amino acid sequence of SEQ ID NO:393; a RSV phosphoprotein P, *e.g.*, having an amino acid sequence of SEQ ID NO:394; an RSV attachment glycoprotein G, *e.g.*, having an amino acid sequence of SEQ ID NO:395; a RSV nucleocapsid protein, *e.g.*, having an amino acid sequence of SEQ ID NO:396; a RSV nucleoprotein (N), *e.g.*, having an amino acid sequence of SEQ ID NO:397; and/or a RSV matrix protein, *e.g.*, having an amino acid sequence of SEQ ID NO:398.

In certain embodiments, the anti-RSV-antigen antibody binds immunospecifically to a protein/polypeptide that consists of an amino acid sequence that is at least 60%, 70%, 80%, 90%, 95%, or at least 98% identical to the amino acid sequence of the attachment glycoprotein of SEQ ID NO:390; the fusion glycoprotein of SEQ ID NO:391; the small hydrophobic protein of SEQ ID NO:392; the RNA polymerase beta subunit (Large structural protein) (L protein) of SEQ ID NO:393; the phosphoprotein P of SEQ ID NO:394; the attachment glycoprotein G of SEQ ID NO:395; the nucleocapsid protein of SEQ ID NO:396; the nucleoprotein (N)of SEQ ID NO:397; and/or the matrix protein of SEQ ID NO:398. In certain embodiments, the anti-RSV-antigen antibody binds immunospecifically to a protein/polypeptide that consists of an amino acid sequence that is at most 70%, 80%, 90%, 95%, 98% or at most 100% identical to the amino acid sequence of the attachment glycoprotein of SEQ ID NO:390; the fusion glycoprotein of SEQ ID NO:391; the small hydrophobic protein of SEQ ID NO:392; the RNA polymerase beta subunit (Large structural protein) (L protein) of SEQ ID NO:393; the phosphoprotein P of SEQ ID NO:394; the attachment glycoprotein G of SEQ ID NO:395; the nucleocapsid protein of SEQ ID NO:396; the nucleoprotein (N)of SEQ ID NO:397; and/or the matrix protein of SEQ ID NO:398.

In certain embodiments, the anti-RSV-antigen antibodies are the anti-RSV-antigen antibodies of or are prepared by the methods of U.S. Application No: 09/724,531, filed November 28, 2000; 09/996,288, filed November 28, 2001; and 09/996,265, filed November 28, 2001, all entitled "Methods of Administering/Dosing Anti-RSV Antibodies for Prophylaxis and Treatment", by Young et al., which are incorporated by reference herein in their entireties. Methods and composition for stabilized antibody formulations that can be used in the methods of the present invention are disclosed in U.S. Provisional Application Nos.: 60/388,921, filed June 14, 2002, and 60/388,920, filed June 14, 2002, which are incorporated by reference herein in their entireties.

In certain embodiments, the one or more antibodies or antigen-binding fragments thereof that bind immunospecifically to a RSV antigen comprise a Fc domain with a higher affinity for the FcRn receptor than the Fc domain of SYNAGIS® (Palivizumab). Such antibodies are described in U.S. Patent Application No.: 10/020,354, filed December 12, 2001, which is incorporated herein by reference in its entireties.

In certain embodiments, the one or more anti-RSV-antigen antibodies include, but are not limited to, SYNAGIS® (Palivizumab). In certain embodiments, the one or more anti-RSV-antigen antibodies include, but are not limited to, A4B4 (see section 4.1.5). In certain specific embodiments, the anti-RSV-antigen antibody is AFFF; P12f2 P12f4; P11d4; Ale9; A12a6; A13c4; A17d4; A4B4; 1X-493L1; FR H3-3F4; M3H9; Y10H6; DG; AFFF(1); 6H8; L1-7E5; L2-15B10; A13a11; A1h5; A4B4(1);A4B4-F52S; or A4B4L1FR-S28R. These antibodies are disclosed in International Application Publication No.: WO 02/43660, entitled "Methods of Administering/Dosing Anti-RSV Antibodies for Prophylaxis and Treatment", by Young et al., which is incorporated herein by reference in its entirety.

In certain embodiments, the one or more antibodies that bind to a RSV antigen has a higher avidity and/or affinity for a RSV antigen than SYNAGIS® has for the RSV F glycoprotein. In certain embodiments, the one or more antibodies that bind immunospecifically to a RSV antigen has a higher affinity and/or avidity for a RSV antigen than any previously known anti-RSV-antigen specific antibodies or antigen-binding fragments thereof. In certain embodiments, anti-RSV-antigen antibody is not SYNAGIS®.

For the methods of the present invention, antibodies or antigen-binding fragments thereof which immunospecifically bind to a RSV antigen with an affinity constant of at least $2 \times 10^8\ M^{-1}$, at least $2.5 \times 10^8\ M^{-1}$, at least $5 \times 10^8\ M^{-1}$, at least $10^9\ M^{-1}$, at least $5 \times 10^9\ M^{-1}$, at least $10^{10}\ M^{-1}$, at least $5 \times 10^{10}\ M^{-1}$, at least $10^{11}\ M^{-1}$, at least $5 \times 10^{11}\ M^{-1}$, at least $10^{12}\ M^{-}$

^{1}, at least 5 X 10^{12} M^{-1}, at least 10^{13} M^{-1}, at least 5 X 10^{13} M^{-1}, at least 10^{14} M^{-1}, at least 5 X 10^{14} M^{-1}, at least 10^{15} M^{-1}, or at least 5 X 10^{15} M^{-1} can be used. In a specific embodiment, the antibody that binds immunospecifically to a RSV antigen is SYNAGIS®, which binds to the RSV F glycoprotein. The present invention also provides pharmaceutical compositions comprising (i) one or more antibodies which immunospecifically bind to a RSV antigen with an affinity constant of at least 2 X 10^{8} M^{-1}, at least 2.5 X 10^{8} M^{-1}, at least 5 X 10^{8} M^{-1}, at least 10^{9} M^{-1}, at least 5 X 10^{9} M^{-1}, at least 10^{10} M^{-1}, at least 5 X 10^{10} M^{-1}, at least 10^{11} M^{-1}, at least 5 X 10^{11} M^{-1}, at least 10^{12} M^{-1}, at least 5 X 10^{12} M^{-1}, at least 10^{13} M^{-1}, at least 5 X 10^{13} M^{-1}, at least 10^{14} M^{-1}, at least 5 X 10^{14} M^{-1}, at least 10^{15} M^{-1}, or at least 5 X 10^{15} M^{-1} and (ii) one or more antibodies which immunospecifically bind to a RSV antigen with an affinity constant of at least 2 X 10^{8} M^{-1}, at least 2.5 X 10^{8} M^{-1}, at least 5 X 10^{8} M^{-1}, at least 10^{9} M^{-1}, at least 5 X 10^{9} M^{-1}, at least 10^{10} M^{-1}, at least 5 X 10^{10} M^{-1}, at least 10^{11} M^{-1}, at least 5 X 10^{11} M^{-1}, at least 10^{12} M^{-1}, at least 5 X 10^{12} M^{-1}, at least 10^{13} M^{-1}, at least 5 X 10^{13} M^{-1}, at least 10^{14} M^{-1}, at least 5 X 10^{14} M^{-1}, at least 10^{15} M^{-1}, or at least 5 X 10^{15} M^{-1}.

It should be recognized that antibodies that immunospecifically bind to a RSV antigen are known in the art. For example, SYNAGIS® is a humanized monoclonal antibody presently used for the prevention of RSV infection in pediatric patients. In a specific embodiment, an antibody to be used with the methods of the present invention is SYNAGIS® or an antibody-binding fragment thereof (*e.g.*, contains one or more complementarity determining regions (CDRs) and preferably, the variable domain of SYNAGIS®). The amino acid sequence of SYNAGIS® is disclosed, *e.g.*, in Johnson et al., 1997, J. Infectious Disease 176:1215-1224, and U.S. Patent No. 5,824,307 and International Application Publication No.: WO 02/43660, entitled "Methods of Administering/Dosing Anti-RSV Antibodies for Prophylaxis and Treatment", by Young et al., which are incorporated herein by reference in their entireties.

In certain embodiments, the antibodies to be used with the methods and compositions of the invention or fragments thereof bind immunospecifically to one or more RSV antigens regardless of the strain of RSV. In particular, the anti-RSV-antigen antibodies bind to an antigen of human RSV A and human RSV B. In certain embodiments, the anti-RSV-antigen antibodies bind to RSV antigens from one strain of RSV versus another RSV strain. In particular, the anti-RSV-antigen antibody binds to an antigen of human RSV A and not to human RSV B or vice versa. In a specific embodiment, the antibodies or antigen-binding fragments thereof immunospecifically bind to the RSV F glycoprotein, G glycoprotein or SH

protein. In certain embodiments, the anti-RSV-antigen antibodies bind immunospecifically to the RSV F glycoprotein. In another preferred embodiment, the anti-RSV-antigen antibodies or antigen-binding fragments thereof bind to the A, B, C, I, II, IV, V, or VI antigenic sites of the RSV F glycoprotein (see, *e.g.*, López et al., 1998, J. Virol. 72:6922-6928, which is incorporated herein by reference in its entirety). In certain embodiments, the anti-RSV-antigen antibodies bind to a RSV nucleoprotein, a RSV phosphoprotein, a RSV matrix protein, a RSV small hydrophobic protein, a RSV RNA-dependent RNA polymerase, a RSV F protein, or a RSV G protein.

In certain embodiments, the anti-RSV-antigen antibodies or antigen-binding fragments thereof have a high binding affinity for one or more RSV antigens. In a specific embodiment, an anti-RSV antibody or an antigen-binding fragment thereof has an association rate constant or k_{on} rate (antibody (Ab) + antigen $(Ag)^{k_{on}} \rightarrow Ab\text{-}Ag)$ <|<BOX1>|>of at least $10^5\ M^{-1}s^{-1}$, at least $5 \times 10^5\ M^{-1}s^{-1}$, at least $10^6\ M^{-1}s^{-1}$, at least $5 \times 10^6\ M^{-1}s^{-1}$, at least $10^7\ M^{-1}s^{-1}$, at least $5 \times 10^7\ M^{-1}s^{-1}$, or at least $10^8\ M^{-1}s^{-1}$. In a preferred embodiment, an antibody of the present invention or fragment thereof has a k_{on} of at least $2 \times 10^5\ M^{-1}s^{-1}$, at least $5 \times 10^5\ M^{-1}s^{-1}$, at least $10^6\ M^{-1}s^{-1}$, at least $5 \times 10^6\ M^{-1}s^{-1}$, at least $10^7\ M^{-1}s^{-1}$, at least $5 \times 10^7\ M^{-1}s^{-1}$, or at least $10^8\ M^{-1}s^{-1}$.

In another embodiment, anti-RSV-antigen antibodies or fragment thereof has a k_{off} rate (antibody (Ab) + antigen) of less than $10^{-1}\ s^{-1}$, less than $5 \times 10^{-1}\ s^{-1}$, less than $10^{-2}\ s^{-1}$, less than $5 \times 10^{-2}\ s^{-1}$, less than $10^{-3}\ s^{-1}$, less than $5 \times 10^{-3}\ s^{-1}$, less than $10^{-4}\ s^{-1}$, less than $5 \times 10^{-4}\ s^{-1}$, less than $10^{-5}\ s^{-1}$, less than $5 \times 10^{-5}\ s^{-1}$, less than $10^{-6}\ s^{-1}$, less than $5 \times 10^{-6}\ s^{-1}$, less than $10^{-7}\ s^{-1}$, less than $5 \times 10^{-7}\ s^{-1}$, less than $10^{-8}\ s^{-1}$, less than $5 \times 10^{-8}\ s^{-1}$, less than $10^{-9}\ s^{-1}$, less than $5 \times 10^{-9}\ s^{-1}$, or less than $10^{-10}\ s^{-1}$. In a preferred embodiment, an anti-RSV-antigen antibodies or fragment thereof has a k_{on} of less than $5 \times 10^{-4}\ s^{-1}$, less than $10^{-5}\ s^{-1}$, less than $5 \times 10^{-5}\ s^{-1}$, less than $10^{-6}\ s^{-1}$, less than $5 \times 10^{-6}\ s^{-1}$, less than $10^{-7}\ s^{-1}$, less than $5 \times 10^{-7}\ s^{-1}$, less than $10^{-8}\ s^{-1}$, less than $5 \times 10^{-8}\ s^{-1}$, less than $10^{-9}\ s^{-1}$, less than $5 \times 10^{-9}\ s^{-1}$, or less than $10^{-10}\ s^{-1}$.

In certain embodiments, the antibodies to be used with the methods of the invention or fragments thereof comprise the amino acid sequence of SYNAGIS® with one or more amino acid residue substitutions in one or more VL CDRs and/or one or more VH CDRs. In a specific embodiment, an antibody to be used with the methods of the invention comprises the amino acid sequence of SYNAGIS® with one or more amino acid residue substitutions of the amino acid residues indicated in bold face and underlining in Table 3. In accordance with this embodiment, the amino acid residue substitutions can be conservative or non-

conservative. The antibody or antibody fragment generated by introducing substitutions in the VH domain, VH CDRs, VL domain and/or VL CDRs of SYNAGIS® can be tested *in vitro* and *in vivo,* for example, for its ability to bind to RSV F antigen, for its ability to neutralize RSV, or for its ability to prevent, treat or ameliorate one or more symptoms associated with a RSV infection.

TABLE 3. CDR Sequences Of SYNAGIS®

CDR	Sequence
VH1	T**S**GMSVG
VH2	DIWWD**D**K**KD**YNPSLK**S**
VH3	**S**MI**T**N**W**YFDV
VL1	**KCQLS**VGYMH
VL2	DT**SKLA**S
VL3	FQGS**G**YP**F**T

Bold faced & underlined amino acid residues are preferred residues which should be substituted.

In certain specific embodiments, the amino acid sequences of the different domains of one or more anti-RSV-antigen antibodies are as follows: **VH Domain:** SEQ ID NO:422; **VH CDR1:** T**A**GMSVG; **VH CDR2:** DIWWDDKK**H**YNPSLK**D**; **VH CDR3:** **D**MI**F**N**F**YFDV; **VL Domain:** SEQ ID NO:423; **VL CDR1:** **SASSR**VGYMH; **VL CDR2:** DT**LL**L**D**S; **VL CDR3:** FQGSGYPFT. This antibody has been disclosed as A4B4(1) in International Application Publication No.: WO 02/43660, entitled "Methods of Administering/Dosing Anti-RSV Antibodies for Prophylaxis and Treatment", by Young et al., which is incorporated by reference herein in its entirety.

In certain specific embodiments, the anti-RSV-antigen antibody is AFFF; P12f2 P12f4; P11d4; Ale9; A12a6; A13c4; A17d4; A4B4; 1X-493L1; FR H3-3F4; M3H9; Y10H6; DG; AFFF(1); 6H8; L1-7E5; L2-15B10; A13a11; A1h5; A4B4(1);A4B4-F52S; or A4B4L1FR-S28R. These antibodies are disclosed in International Application Publication No.: WO 02/43660, entitled "Methods of Administering/Dosing Anti-RSV Antibodies for Prophylaxis and Treatment", by Young et al., which is incorporated herein by reference in its entirety.

4.1.7 ANTI-HMPV-ANTIGEN ANTIBODIES

Any antibody that immunospecifically binds to an hMPV or to a protein of hMPV or a fragment, an analog, a derivative or a homolog thereof can be used with the methods of the

invention. Mammalian MPV and proteins of mammalian MPV and homologs thereof are described in section 4.1.7.1.

4.1.7.1 hMPV

STRUCTURAL CHARACTERISTICS OF A MAMMALIAN METAPNEUMOVIRUS

A Mammalian MPV is a negative-sense single stranded RNA virus belonging to the sub-family *Pneumovirinae* of the family Paramyxoviridae. Moreover, the mammalian MPV is identifiable as phylogenetically corresponding to the genus Metapneumovirus, wherein the mammalian MPV is phylogenetically more closely related to a virus isolate deposited as I-2614 with CNCM, Paris (SEQ ID NO:19) than to turkey rhinotracheitis virus, the etiological agent of avian rhinotracheitis. A virus is identifiable as phylogenetically corresponding to the genus *Metapneumovirus* by, *e.g.*, obtaining nucleic acid sequence information of the virus and testing it in phylogenetic analyses. Any technique known to the skilled artisan can be used to determine phylogenetic relationships between strains of viruses. Other techniques are disclosed in International Patent Application PCT/NL02/00040, published as WO 02/057302, which is incorporated by reference in its entirety herein. In particular, PCT/NL02/00040 discloses nucleic acid sequences that are suitable for phylogenetic analysis at page 12, line 27 to page 19, line 29, which are incorporated by reference herein. A virus can further be identified as a mammalian MPV on the basis of sequence similarity as described in more detail below.

In a specific embodiment, the mammalian MPV is a human MPV.

In addition to phylogenetic relatedness and sequence similarity of a virus to a mammalian MPV as disclosed herein, the similarity of the genomic organization of a virus to the genomic organization of a mammalian MPV disclosed herein can also be used to identify the virus as a mammalian MPV. In certain embodiments, the genomic organization of a mammalian MPV is different from the genomic organization of pneumoviruses within the sub-family *Pneumovirinae* of the family *Paramyxoviridae*. The classification of the two genera, metapneumovirus and pneumovirus, is based primarily on their gene constellation; metapneumoviruses generally lack non-structural proteins such as NS1 or NS2 (*see* also Randhawa *et al.*, 1997, J. Virol. 71:9849-9854) and the gene order is different from that of pneumoviruses (RSV: '3-NS1-NS2-N-P-M-SH-G-F-M2-L-5', APV:

'3-N-P-M-F-M2-SH-G-L-5') (Lung, *et al.*, 1992, J. Gen. Virol. 73:1709-17 15; Yu, *et al.*, 1992, *Virology* 186:426-434; Randhawa, *et al.*, 1997, J. Virol. 71:9849-9854).

Further, a mammalian MPV of the invention can be identified by its immunological properties. In certain embodiments, specific anti-sera can be raised against mammalian MPV that can neutralize mammalian MPV. Monoclonal and polyclonal antibodies can be raised against MPV that can also neutralize mammalian MPV. (*See*, WO 02/057302, which is incorporated by reference herein.

The mammalian MPV of the invention is further characterized by its ability to infect a mammalian host, *i.e.*, a mammalian cultured cell or a mammal. Unlike APV, mammalian MPV does not replicate or replicates only at low levels in chickens and turkeys. Mammalian MPV replicates, however, in mammalian hosts, such as cynomolgous macaques. In certain, more specific, embodiments, a mammalian MPV is further characterized by its ability to replicate in a mammalian host. In certain, more specific embodiments, a mammalian MPV is further characterized by its ability to cause the mammalian host to express proteins encoded by the genome of the mammalian MPV. In even more specific embodiments, the viral proteins expressed by the mammalian MPV are inserted into the cytoplasmic membranes of the mammalian host. In certain embodiments, the mammalian MPV of the invention can infect a mammalian host and cause the mammalian host to produce new infectious viral particles of the mammalian MPV. For a more detailed description of the functional characteristics of the mammalian MPV of the invention, see below.

In certain embodiments, the appearance of a virus in an electron microscope or its sensitivity to chloroform can be used to identify the virus as a mammalian MPV. The mammalian MPV of the invention appears in an electron microscope as paramyxovirus-like particle. Consistently, a mammalian MPV is sensitive to treatment with chloroform; a mammalian MPV is cultured optimally on tMK cells or cells functionally equivalent thereto and it is essentially trypsine dependent in most cell cultures. Furthermore, a mammalian MPV has a typical cytopathic effects (CPE) and lacks haemagglutinating activity against species of red blood cells. The CPE induced by MPV isolates are similar to the CPE induced by hRSV, with characteristic syncytia formation followed by rapid internal disruption of the cells and subsequent detachment from the culture plates. Although most paramyxoviruses have haemagglutinating activity, most of the pneumoviruses do not (Pringle, C.R. In: *The Paramyxoviruses*; (ed. D.W. Kingsbury) 1-39 (Plenum Press, New York, 1991)). A mammalian MPV contains a second overlapping ORF (M2-2) in the nucleic acid fragment

encoding the M2 protein. The occurrence of this second overlapping ORF occurs in other pneumoviruses as shown in Ahmadian *et al.*, 1999, *J. Gen. Vir.* 80:2011-2016.

In certain embodiments, a viral isolate can be identified as a mammalian MPV by the following method. A test sample can, *e.g.*, be obtained from an animal or human. The sample is then tested for the presence of a virus of the sub-family *Pneumovirinae*. If a virus of the sub-family *Pneumovirinae* is present, the virus can be tested for any of the characteristics of a mammalian MPV as discussed herein, such as, but not limited to, phylogenetic relatedness to a mammalian MPV, nucleotide sequence identity to a nucleotide sequence of a mammalian MPV, amino acid sequence identity/homology to a amino acid sequence of a mammalian MPV, and genomic organization. Furthermore, the virus can be identified as a mammalian MPV by cross-hybridization experiments using nucleic acid sequences from a MPV isolate, RT-PCR using primers specific to mammalian MPV, or in classical cross-serology experiments using antibodies directed against a mammalian MPV isolate. In certain other embodiments, a mammalian MPV can be identified on the basis of its immunological distinctiveness, as determined by quantitative neutralization with animal antisera. The antisera can be obtained from, *e.g.*, ferrets, pigs or macaques that are infected with a mammalian MPV.

In certain embodiments, the serotype does not cross-react with viruses other than mammalian MPV. In other embodiments, the serotype shows a homologous-to-heterologous titer ratio >16 in both directions If neutralization shows a certain degree of cross-reaction between two viruses in either or both directions (homologous-to-heterologous titer ration of eight or sixteen), distinctiveness of serotype is assumed if substantial biophysical/biochemical differences of DNA sequences exist. If neutralization shows a distinct degree of cross-reaction between two viruses in either or both directions (homologous-to-heterologous titer ratio of smaller than eight), identity of serotype of the isolates under study is assumed. Isolate I-2614, herein also known as MPV isolate 00-1 (as deposited with CNCM, Paris (SEQ ID NO:19)), can be used as prototype.

In certain embodiments, a virus can be identified as a mammalian MPV by means of sequence homology/identity of the viral proteins or nucleic acids in comparison with the amino acid sequence and nucleotide sequences of the viral isolates disclosed herein by sequence or deposit. In particular, a virus is identified as a mammalian MPV when the genome of the virus contains a nucleic acid sequence that has a percentage nucleic acid identity to a virus isolate deposited as I-2614 with CNCM, Paris which is higher than the

percentages identified herein for the nucleic acids encoding the L protein, the M protein, the N protein, the P protein, or the F protein as identified herein below in comparison with APV-C (see Table 4). (See, PCT WO 02/05302, at pp. 12 to 19, which is incorporated by reference herein. Without being bound by theory, it is generally known that viral species, especially RNA virus species, often constitute a quasi species wherein the members of a cluster of the viruses display sequence heterogeneity. Thus, it is expected that each individual isolate may have a somewhat different percentage of sequence identity when compared to APV-C.

The highest amino sequence identity between the proteins of MPV and any of the known other viruses of the same family to date is the identity between APV-C and human MPV. Between human MPV and APV-C, the amino acid sequence identity for the matrix protein is 87%, 88% for the nucleoprotein, 68% for the phosphoprotein, 81% for the fusion protein and 56-64% for parts of the polymerase protein, as can be deduced when comparing the sequences given in Figure 30, see also Table 4. Viral isolates that contain ORFs that encode proteins with higher homology compared to these maximum values are considered mammalian MPVs. It should be noted that, similar to other viruses, a certain degree of variation is found between different isolated of mammalian MPVs.

TABLE 4: Amino acid sequence identity between the ORFs of MPV and those of other paramyxoviruses .

	N	P	M	F	M2-1	M2-2	L
APV A	69	55	78	67	72	26	64
APV B	69	51	76	67	71	27	-[2]
APV C	88	68	87	81	84	56	-[2]
hRSVA	42	24	38	34	36	18	42
hRSV B	41	23	37	33	35	19	44
bRSV	42	22	38	34	35	13	44
PVM	45	26	37	39	33	12	-[2]
others[3]	7-11	4-9	7-10	10-18	-[4]	-[4]	13-14

Footnotes:

1. No sequence homologies were found with known G and SH proteins and were thus excluded

2. Sequences not available.

3. others: human parainfluenza virus type 2 and 3, Sendai virus, measles virus, nipah virus, phocine distemper virus, and New Castle Disease virus.

4. ORF absent in viral genome.

Any protein of a mammalian MPV can be used as an immunogen to generate antibodies to be used with the methods of the invention. In certain embodiments, an antibody to be used with the methods of treatment of the present invention bind immunospecifically to a protein of mammlian MPV as set forth below.

In certain embodiments, the amino acid sequence of the SH protein of the mammalian MPV is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 99.5% identical to the amino acid sequence of SEQ ID NO:382 (SH protein of isolate NL/1/00; see Table 5). The isolated negative-sense single stranded RNA metapneumovirus that comprises the SH protein that is at least 30% identical to SEQ ID NO:382 (SH protein of isolate NL/1/00; see Table 5) is capable of infecting a mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the SH protein that is at least 30% identical to SEQ ID NO:382 (SH protein of isolate NL/1/00; see Table 5) is capable of replicating in a mammalian host. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a SH protein that is at least 30% identical to SEQ ID NO:382 (SH protein of isolate NL/1/00; see Table 5).

In certain embodiments, the amino acid sequence of the G protein of the mammalian MPV is at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 99.5% identical to the amino acid sequence of SEQ ID NO:322 (G protein of isolate NL/1/00; see Table 5). The isolated negative-sense single stranded RNA metapneumovirus that comprises the G protein that is at least 20% identical to SEQ ID NO:322 (G protein of isolate NL/1/00; see Table 5) is capable of infecting a mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the G protein that is at least 20% identical to SEQ ID NO:322 (G protein of isolate NL/1/00; see Table 5) is capable of replicating in a mammalian host. In certain embodiments, a mammalian MPV contains a

nucleotide sequence that encodes a G protein that is at least 20% identical to SEQ ID NO:322 (G protein of isolate NL/1/00; see Table 5).

In certain embodiments, the amino acid sequence of the L protein of the mammalian MPV is at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 99.5% identical to the amino acid sequence of SEQ ID NO:330 (L protein of isolate NL/1/00; see Table 5). The isolated negative-sense single stranded RNA metapneumovirus that comprises the L protein that is at least 85% identical to SEQ ID NO:330 (L protein of isolate NL/1/00; see Table 5) is capable of infecting a mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the L protein that is at least 85% identical to SEQ ID NO:330 (L protein of isolate NL/1/00; see Table 5) is capable of replicating in a mammalian host. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a L protein that is at least 20% identical to SEQ ID NO:330 (L protein of isolate NL/1/00; see Table 5).

In certain embodiments, the amino acid sequence of the N protein of the mammalian MPV is at least 90%, at least 95%, or at least 98% identical to the amino acid sequence of SEQ ID NO:366. The isolated negative-sense single stranded RNA metapneumovirus that comprises the N protein that is at least 90% identical in amino acid sequence to SEQ ID NO:366 is capable of infecting mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the N protein that is 90% identical in amino acid sequence to SEQ ID NO:366 is capable of replicating in a mammalian host. The amino acid identity is calculated over the entire length of the N protein. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a N protein that is at least 90%, at least 95%, or at least 98% identical to the amino acid sequence of SEQ ID NO:366.

The amino acid sequence of the P protein of the mammalian MPV is at least 70%, at least 80%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:374. The mammalian MPV that comprises the P protein that is at least 70% identical in amino acid sequence to SEQ ID NO:374 is capable of infecting a mammalian host. In certain embodiments, the mammalian MPV that comprises the P protein that is at least 70% identical in amino acid sequence to SEQ ID NO:374 is capable of replicating in a mammalian host. The amino acid identity is calculated over the entire length of the P protein. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a P

protein that is at least 70%, at least 80%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:374.

The amino acid sequence of the M protein of the mammalian MPV is at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:358. The mammalian MPV that comprises the M protein that is at least 90% identical in amino acid sequence to SEQ ID NO:358 is capable of infecting mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the M protein that is 90% identical in amino acid sequence to SEQ ID NO:358 is capable of replicating in a mammalian host. The amino acid identity is calculated over the entire length of the M protein. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a M protein that is at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:358.

The amino acid sequence of the F protein of the mammalian MPV is at least 85%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:314. The mammalian MPV that comprises the F protein that is at least 85% identical in amino acid sequence to SEQ ID NO:314 is capable of infecting a mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the F protein that is 85% identical in amino acid sequence to SEQ ID NO:314 is capable of replicating in mammalian host. The amino acid identity is calculated over the entire length of the F protein. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a F protein that is at least 85%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:314.

The amino acid sequence of the M2-1 protein of the mammalian MPV is at least 85%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:338. The mammalian MPV that comprises the M2-1 protein that is at least 85% identical in amino acid sequence to SEQ ID NO:338 is capable of infecting a mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the M2-1 protein that is 85% identical in amino acid sequence to SEQ ID NO:338 is capable of replicating in a mammalian host. The amino acid identity is calculated over the entire length of the M2-1 protein. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a M2-1 protein that is at least 85%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:338.

The amino acid sequence of the M2-2 protein of the mammalian MPV is at least 60%, at least 70%, at least 80%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:346 The isolated mammalian MPV that comprises the M2-2 protein that is at least 60% identical in amino acid sequence to SEQ ID NO:346 is capable of infecting mammalian host. In certain embodiments, the isolated negative-sense single stranded RNA metapneumovirus that comprises the M2-2 protein that is 60% identical in amino acid sequence to SEQ ID NO:346 is capable of replicating in a mammalian host. The amino acid identity is calculated over the entire length of the M2-2 protein. In certain embodiments, a mammalian MPV contains a nucleotide sequence that encodes a M2-1 protein that is is at least 60%, at least 70%, at least 80%, at least 90%, at least 95% or at least 98% identical to the amino acid sequence of SEQ ID NO:346.

In certain embodiments, the negative-sense single stranded RNA metapneumovirus encodes at least two proteins, at least three proteins, at least four proteins, at least five proteins, or six proteins selected from the group consisting of (i) a N protein with at least 90% amino acid sequence identity to SEQ ID NO:366; (ii) a P protein with at least 70% amino acid sequence identity to SEQ ID NO:374 (iii) a M protein with at least 90% amino acid sequence identity to SEQ ID NO:358 (iv) a F protein with at least 85% amino acid sequence identity to SEQ ID NO:314 (v) a M2-1 protein with at least 85% amino acid sequence identity to SEQ ID NO:338; and (vi) a M2-2 protein with at least 60% amino acid sequence identity to SEQ ID NO:346.

Mammalian MPV, can be divided into two subgroups, subgroup A and subgroup B, and the two subgroups can each be devided into two variants, A1 and A2, and B1 and B2. A mammalian MPV can be identified as a member of subgroup A if it is phylogenetically closer related to the isolate 00-1 (SEQ ID NO:19) than to the isolate 99-1 (SEQ ID NO:18). A mammalian MPV can be identified as a member of subgroup B if it is phylogenetically closer related to the isolate 99-1 (SEQ ID NO:18) than to the isolate 00-1 (SEQ ID NO:19). In other embodiments, nucleotide or amino acid sequence homologies of individual ORFs can be used to classify a mammalian MPV as belonging to subgroup A or B.

The different isolates of mammalian MPV can be divided into four different variants, variant A1, variant A2, variant B1 and variant B2 (*see*Figures 21 and 22). The isolate 00-1 (SEQ ID NO:19) is an example of the variant A1 of mammalian MPV. The isolate 99-1 (SEQ ID NO:18) is an example of the variant B1 of mammalian MPV. A mammalian MPV can be grouped into one of the four variants using a phylogenetic analysis. Thus, a

mammalian MPV belongs to a specific variant if it is phylogenetically closer related to a known member of that variant than it is phylogenetically related to a member of another variant of mammalian MPV. The sequence of any ORF and the encoded polypeptide may be used to type a MPV isolate as belonging to a particular subgroup or variant, including N, P, L, M, SH, G, M2 or F polypeptides. In a specific embodiment, the classification of a mammalian MPV into a variant is based on the sequence of the G protein. Without being bound by theory, the G protein sequence is well suited for phylogenetic analysis because of the high degree of variation among G proteins of the different variants of mammalian MPV.

In certain embodiments of the invention, sequence homology may be determined by the ability of two sequences to hybridize under certain conditions, as set forth below. A nucleic acid which is hybridizable to a nucleic acid of a mammalian MPV, or to its reverse complement, or to its complement can be used in the methods of the invention to determine their sequence homology and identities to each other. In certain embodiments, the nucleic acids are hybridized under conditions of high stringency.

It is well-known to the skilled artisan that hybridization conditions, such as, but not limited to, temperature, salt concentration, pH, formamide concentration (*see*, e.g., Sambrook et al., 1989, Chapters 9 to 11, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, incorporated herein by reference in its entirety) . In certain embodiments, hybridization is performed in aqueous solution and the ionic strength of the solution is kept constant while the hybridization temperature is varied dependent on the degree of sequence homology between the sequences that are to be hybridized. For DNA sequences that 100% identical to each other and are longer than 200 basebairs, hybridization is carried out at approximately 15-25°C below the melting temperature (Tm) of the perfect hybrid. The melting temperature (Tm) can be calculated using the following equation (Bolton and McCarthy, 1962, Proc. Natl. Acad. Sci. USA 84:1390):

$$Tm = 81.5°C - 16.6(\log10[Na+]) + (\%G+C) - 0.63(\%formamide) - (600/l)$$

Wherein (Tm) is the melting temperature, [Na+] is the sodium concentration, G+C is the Guanine and Cytosine content, and l is the length of the hybrid in basepairs. The effect of mismatches between the sequences can be calculated using the formula by Bonner et al. (Bonner et al., 1973, J. Mol. Biol. 81:123-135): for every 1% of mismatching of bases in the hybrid, the melting temperature is reduced by 1-1.5°C.

Thus, by determining the temperature at which two sequences hybridize, one of skill in the art can estimate how similar a sequence is to a known sequence. This can be done, e.g., by comparison of the empirically determined hybridization temperature with the hybridization temperature calculated for the know sequence to hybridize with its perfect match. Through the use of the formula by Bonner et al., the relationship between hybridization temperature and per cent mismatch can be exploited to provide information about sequence similarity.

By way of example and not limitation, procedures using such conditions of high stringency are as follows. Prehybridization of filters containing DNA is carried out for 8 h to overnight at 65 C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 μg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65 C in prehybridization mixture containing 100 μg/ml denatured salmon sperm DNA and 5-20 X 106 cpm of 32P-labeled probe. Washing of filters is done at 37 C for 1 h in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 C for 45 min before autoradiography. Other conditions of high stringency which may be used are well known in the art. In other embodiments of the invention, hybridization is performed under moderate of low stringency conditions, such conditions are well-known to the skilled artisan (*see* e.g., Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York; see also, Ausubel et al., eds., in the Current Protocols in Molecular Biology series of laboratory technique manuals, 1987-1997 Current Protocols,© 1994-1997 John Wiley and Sons, Inc., each of which is incorporated by reference herein in their entirety). An illustrative low stringency condition is provided by the following system of buffers: hybridization in a buffer comprising 35% formamide, 5X SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 μg/ml denatured salmon sperm DNA, and 10% (wt/vol) dextran sulfate for 18-20 hours at 40□C, washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 55□C, and washing in a buffer consisting of 2X SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS for 1.5 hours at 60□C.

In certain embodiments, a mammalian MPV can be classified into one of the variant using probes that are specific for a specific variant of mammalian MPV. Such probes include primers for RT-PCR (Table 5) and antibodies.

In certain embodiments of the invention, the different variants of mammalian MPV can be distinguished from each other by way of the amino acid sequences of the different viral proteins. In other embodiments, the different variants of mammalian MPV can be distinguished from each other by way of the nucleotide sequences of the different ORFs encoded by the viral genome. A variant of mammalian MPV can be, but is not limited to, A1, A2, B1 or B2.

An isolate of mammalian MPV is classified as a variant B1 if it is phylogenetically closer related to the viral isolate NL/1/99 (SEQ ID NO:18) than it is related to any of the following other viral isolates: NL/1/00 (SEQ ID NO:19), NL/17/00 (SEQ ID NO:20) and NL/1/94 (SEQ ID NO:21). One or more of the ORFs of a mammalian MPV can be used to classify the mammalian MPV into a variant. A mammalian MPV can be classified as an MPV variant B1, if the amino acid sequence of its G protein is at least 66%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% or at least 99.5% identical to the G protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:324); if the amino acid sequence of its N proteint is at least 98.5% or at least 99% or at least 99.5% identical to the N protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:368); if the amino acid sequence of its P protein is at least 96%, at least 98%, or at least 99% or at least 99.5% identical to the P protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:376); if the amino acid sequence of its M protein is identical to the M protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:360); if the amino acid sequence of its F protein is at least 99% identical to the F protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:316); if the amino acid sequence of its M2-1 protein is at least 98% or at least 99% or at least 99.5% identical to the M2-1 protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:340); if the amino acid sequence of its M2-2 protein is at least 99%or at least 99.5% identical to the M2-2 protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:348); if the amino acid sequence of its SH protein is at least 83%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% or at least 99.5% identical to the SH protein of a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:384); and/or if the amino acid sequence of its L protein is at least 99% or at least 99.5% identical to the L protein a mammalian MPV variant B1 as represented by the prototype NL/1/99 (SEQ ID NO:332).

An isolate of mammalian MPV is classified as a variant A1 if it is phylogenetically closer related to the viral isolate NL/1/00 (SEQ ID NO:19) than it is related to any of the following other viral isolates: NL/1/99 (SEQ ID NO:18), NL/17/00 (SEQ ID NO:20) and NL/1/94 (SEQ ID NO:21). One or more of the ORFs of a mammalian MPV can be used to classify the mammalian MPV into a variant. A mammalian MPV can be classified as an MPV variant A1, if the amino acid sequence of its G protein is at least 66%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% or at least 99.5% identical to the G protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:322); if the amino acid sequence of its N protein is at least 99.5% identical to the N protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:366); if the amino acid sequence of its P protein is at least 96%, at least 98%, or at least 99% or at least 99.5% identical to the P protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:374); if the amino acid sequence of its M protein is at least 99% or at least 99.5% identical to the M protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:358); if the amino acid sequence of its F protein is at least 98% or at least 99% or at least 99.5% identical to the F protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:314); if the amino acid sequence of its M2-1 protein is at least 99% or at least 99.5% identical to the M2-1 protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:338); if the amino acid sequence of its M2-2 protein is at least 96% or at least 99% or at least 99.5% identical to the M2-2 protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:346); if the amino acid sequence of its SH protein is at least 84%, at least 90%, at least 95%, at least 98%, or at least 99% or at least 99.5% identical to the SH protein of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:382); and/or if the amino acid sequence of its L protein is at least 99% or at least 99.5% identical to the L protein of a virus of a mammalian MPV variant A1 as represented by the prototype NL/1/00 (SEQ ID NO:330).

An isolate of mammalian MPV is classified as a variant A2 if it is phylogenetically closer related to the viral isolate NL/17/00 (SEQ ID NO:20) than it is related to any of the following other viral isolates: NL/1/99 (SEQ ID NO:18), NL/1/00 (SEQ ID NO:19) and NL/1/94 (SEQ ID NO:21). One or more of the ORFs of a mammalian MPV can be used to classify the mammalian MPV into a variant. A mammalian MPV can be classified as an

MPV variant A2, if the amino acid sequence of its G protein is at least 66%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99% or at least 99.5% identical to the G protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:332); if the amino acid sequence of its N protein is at least 99.5% identical to the N protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:367); if the amino acid sequence of its P protein is at least 96%, at least 98%, at least 99% or at least 99.5% identical to the P protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:375); if the amino acid sequence of its M protein is at least 99%, or at least 99.5% identical to the M protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:359); if the amino acid sequence of its F protein is at least 98%, at least 99% or at least 99.5% identical to the F protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:315); if the amino acid sequence of its M2-1 protein is at least 99%, or at least 99.5% identical to the M2-1 protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO: 339); if the amino acid sequence of its M2-2 protein is at least 96%, at least 98%, at least 99% or at least 99.5% identical to the M2-2 protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:347); if the amino acid sequence of its SH protein is at least 84%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99% or at least 99.5% identical to the SH protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:383); if the amino acid sequence of its L protein is at least 99% or at least 99.5% identical to the L protein of a mammalian MPV variant A2 as represented by the prototype NL/17/00 (SEQ ID NO:331).

An isolate of mammalian MPV is classified as a variant B2 if it is phylogenetically closer related to the viral isolate NL/1/94 (SEQ ID NO:21) than it is related to any of the following other viral isolates: NL/1/99 (SEQ ID NO:18), NL/1/00 (SEQ ID NO:19) and NL/17/00 (SEQ ID NO:20). One or more of the ORFs of a mammalian MPV can be used to classify the mammalian MPV into a variant. A mammalian MPV can be classified as an MPV variant B2, if the amino acid sequence of its G protein is at least 66%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% or at least 99.5% identical to the G protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:325); if the amino acid sequence of its N protein is at least 99% or at least 99.5% identical to the N protein of a mammalian MPV variant B2 as

represented by the prototype NL/1/94 (SEQ ID NO:369); if the amino acid sequence of its P protein is at least 96%, at least 98%, or at least 99% or at least 99.5% identical to the P protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:377); if the amino acid sequence of its M protein is identical to the M protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:361); if the amino acid sequence of its F protein is at least 99% or at least 99.5% identical to the F protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:317); if the amino acid sequence of the M2-1 protein is at least 98% or at least 99% or at least 99.5% identical to the M2-1 protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:341); if the amino acid sequence that is at least 99% or at least 99.5% identical to the M2-2 protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:349); if the amino acid sequence of its SH protein is at least 84%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% or at least 99.5% identical to the SH protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:385); and/or if the amino acid sequence of its L protein is at least 99% or at least 99.5% identical to the L protein of a mammalian MPV variant B2 as represented by the prototype NL/1/94 (SEQ ID NO:333).

In certain embodiments, the percentage of sequence identity is based on an alignment of the full length proteins. In other embodiments, the percentage of sequence identity is based on an alignment of contiguous amino acid sequences of the proteins, wherein the amino acid sequences can be 25 amino acids, 50 amino acids, 75 amino acids, 100 amino acids, 125 amino acids, 150 amino acids, 175 amino acids, 200 amino acids, 225 amino acids, 250 amino acids, 275 amino acids, 300 amino acids, 325 amino acids, 350 amino acids, 375 amino acids, 400 amino acids, 425 amino acids, 450 amino acids, 475 amino acids, 500 amino acids, 750 amino acids, 1000 amino acids, 1250 amino acids, 1500 amino acids, 1750 amino acids, 2000 amino acids or 2250 amino acids in length.

FUNCTIONAL CHARACTERISTICS OF A MAMMALIAN MPV

In addition to the structural definitions of the mammalian MPV, a mammalian MPV can also be defined by its functional characteristics. In certain embodiments, a mammalian MPV is capable of infecting a mammalian host. The mammalian host can be a mammalian cell, tissue, organ or a mammal. In a specific embodiment, the mammalian host is a human or a human cell, tissue or organ. Any method known to the skilled artisan can be used to test

whether the mammalian host has been infected with the mammalian MPV. In certain embodiments, the virus is tested for its ability to attach to a mammalian cell. In certain other embodiments, the virus is tested for its ability to transfer its genome into the mammalian cell. In an illustrative embodiment, the genome of the virus is detectably labeled, *e.g.*, radioactively labeled. The virus is then incubated with a mammalian cell for at least 1 minute, at least 5 minutes at least 15 minutes, at least 30 minutes, at least 1 hour, at least 2 hours, at least 5 hours, at least 12 hours, or at least 1 day. The cells are subsequently washed to remove any viral particles from the cells and the cells are then tested for the presence of the viral genome by virtue of the detectable label. In another embodiment, the presence of the viral genome in the cells is detected using RT-PCR using mammalian MPV specific primers. (*See* , PCT WO 02/057302 at pp. 37 to 44, which is incorporated by reference herein).

In certain embodiments, a mammalian virus is capable to infect a mammalian host and to cause proteins of the mammalian MPV to be inserted into the cytoplasmic membrane of the mammalian host. The mammalian host can be a cultured mammalian cell, organ, tissue or mammal. In an illustrative embodiment, a mammalian cell is incubated with the mammalian virus. The cells are subsequently washed under conditions that remove the virus from the surface of the cell. Any technique known to the skilled artisan can be used to detect the newly expressed viral protein inserted in the cytoplasmic membrane of the mammalian cell. For example, after infection of the cell with the virus, the cells are maintained in medium comprising a detectably labeled amino acid. The cells are subsequently harvested, lysed, and the cytoplasmic fraction is separated from the membrane fraction. The proteins of the membrane fraction are then solubilized and then subjected to an immunoprecipitation using antibodies specific to a protein of the mammalian MPV, such as, but not limited to, the F protein or the G protein. The immunoprecipitated proteins are then subjected to SDS PAGE. The presence of viral protein can then be detected by autoradiography. In another embodiment, the presence of viral proteins in the cytoplasmic membrane of the host cell can be detected by immunocytochemistry using one or more antibodies specific to proteins of the mammalian MPV.

In even other embodiments, a mammalian MPV is capable of infecting a mammalian host and of replicating in the mammalian host. The mammalian host can be a cultured mammalian cell, organ, tissue or mammal. Any technique known to the skilled artisan can be used to determine whether a virus is capable of infecting a mammalian cell and of replicating

within the mammalian host. In a specific embodiment, mammalian cells are infected with the virus. The cells are subsequently maintained for at least 30 minutes, at least 1 hour, at least 2 hours, at least 5 hours, at least 12 hours, at least 1 day, or at least 2 days. The level of viral genomic RNA in the cells can be monitored using Northern blot analysis, RT-PCR or *in situ* hybridization using probes that are specific to the viral genome. An increase in viral genomic RNA demonstrates that the virus can infect a mammalian cell and can replicate within a mammalian cell.

In even other embodiments, a mammalian MPV is capable of infecting a mammalian host, wherein the infection causes the mammalian host to produce new infectious mammalian MPV. The mammalian host can be a cultured mammalian cell or a mammal. Any technique known to the skilled artisan can be used to determine whether a virus is capable of infecting a mammalian host and cause the mammalian host to produce new infectious viral particles. In an illustrative example, mammalian cells are infected with a mammalian virus. The cells are subsequently washed and incubated for at least 30 minutes, at least 1 hour, at least 2 hours, at least 5 hours, at least 12 hours, at least 1 day, at least 2 days, at least one week, or at least twelve days. The titer of virus can be monitored by any method known to the skilled artisan. For exemplary methods see section 5.8.

In certain, specific embodiments, a mammalian MPV is a human MPV. The tests described in this section can also be performed with a human MPV. In certain embodiments, the human MPV is capable of infecting a mammalian host, such as a mammal or a mammalian cultured cell.

In certain embodiments, a human MPV is capable to infect a mammalian host and to cause proteins of the human MPV to be inserted into the cytoplasmic membrane of the mammalian host.

In even other embodiments, a human MPV is capable of infecting a mammalian host and of replicating in the mammalian host.

In even other embodiments, the human MPV of the invention is capable of infecting a mammalian host and of replicating in the mammalian host, wherein the infection and replication causes the mammalian host to produce and package new infectious human MPV.

In certain embodiments, a mammalian MPV, even though it is capable of infecting a mammalian host, is also capable of infecting an avian host, such as a bird or an avian cultured cell. In certain embodiments, the mammalian MPV is capable to infect an avian host and to cause proteins of the mammalian MPV to be inserted into the cytoplasmic membrane of the

avian host. In even other embodiments, the mammalian MPV of the invention is capable of infecting an avian host and of replicating in the avian host. In even other embodiments, the mammalian MPV of the invention is capable of infecting an avian host and of replicating in the avian host, wherein the infection and replication causes the avian host to produce and package new infectious mammalian MPV.

A description of mammalian MPV can also be found in co-owned and co-pending U.S. Application Nos.: 10/371,099 and 10/371,122; both filed on February 21, 2003; both of which are incorporated herein by reference in their entireties.

4.1.7.2 Anti-hMPV Antibodies

An anti-hMPV-antigen antibody to be used with the methods of the invention can be an antibody that immunospecifically binds to hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and hMPV G protein.

In certain embodiments, the anti-hMPV-antigen antibody binds immunospecifically to a hMPV antigen of a hMPV isolate from Canadian, to a hMPV isolate from The Netherlands, and/or to a hMPV antigen from a hMPV isolate from Australia. The different isolates are described in Peret et al, 2002, J Infect Dis 185:1660-1663, which is incorporated herein by reference in its entirety.

In certain embodiments, an anti-hMPV-antigen antibody binds to allelic variants of a hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and/or hMPV G protein.

In certain embodiments, an antibody to be used with the methods of treatment of the invention is an antibody that immunospecifically binds to a mammalian MPV, or a protein of a mammalian MPV as described in section 4.1.7.1. In certain embodiments, an antibody to be used with the methods of treatment of the invention is an antibody that immunospecifically binds to a human MPV.

In certain embodiments, the anti-hMPV-antigen antibody binds immunospecifically to a protein/polypeptide that consists, *e.g.*, of an amino acid sequence of SEQ ID NOs: 399-406, 420, or 421, respectively.

In certain embodiments, the anti-hMPV-antigen antibody binds immunospecifically to a protein/polypeptide that consists of an amino acid sequence that is at least 60%, 70%, 80%,

90%, 95%, or at least 98% identical to the amino acid sequence of SEQ ID NOs: 399-406, 420, or 421, respectively. In certain embodiments, the anti-hMPV-antigen antibody binds immunospecifically to a protein/polypeptide that consists of an amino acid sequence that is at most 70%, 80%, 90%, 95%, 98% or at most 100% identical to the amino acid sequence of SEQ ID NOs: 399-406, 420, or 421, respectively.

In certain embodiments, the anti-hMPV-antigen antibody cross reacts with an APV antigen from APV associated with any avian, particularly turkey, duck, or chicken. In certain, more specific embodiments, the anti-hMPV-antibody cross-reacts with an antigen of APV-A, APV-B, APV-C, and/or APV-D, or any combination thereof, particularly turkey APV. In certain more specific embodiments, the anti-hMPV-antigen antibody cross-reacts with an antigen from a European APV isolate. In certain other embodiments, the anti-hMPV-antigen antibody cross-reacts with an antigen from a North American APV isolate. In certain embodiments, the anti-hMPV-antigen antibody cross-reacts with a APV nucleoprotein, APV phosphoprotein, APV matrix protein, APV small hydrophobic protein, APV RNA-dependent RNA polymerase, APV F protein, and/or APV G protein. In certain embodiments, the anti-hMPV-antigen antibody does not cross-react with an APV antigen. In certain embodiments, the anti-hMPV-antigen antibody cross reacts with an APV antigen of an amino acid sequence of, *e.g.*, SEQ ID NO:424 to 429, respectively.

In a specific embodiment, a monoclonal antibody against the F protein of hMPV is generated. In a more specific embodiment, the F protein of hMPV is produced using a baculovirus expression system (*e.g.*, the BD BaculoGold™ Baculovirus Expression Vector System can be used from BD Biosciences, NJ). In certain embodiments, the F protein is expressed without the transmembrane domain to induce secretion of the F protein from the cell in which the protein is expressed. Exemplary expression constructs that can be used for the expression of F protein for the generation of antibodies against the F protein are shown in Figure 1.

In certain embodiments, peptides that contain the following amino acid sequences are used for the generation of antibodies for use with the methods of the invention: amino acid 19 to 28; amino acid 94 to 106; amino acid 476 to 409, and/or amino acid 223 to 236 of SEQ ID NO:234 or SEQ ID NO:279. In certain embodiments, peptides that contain the amino acid sequences of SEQ ID NOs:430-437 are used as immunogens for the generation of antibodies for use with the methods of the invention. Without being bound by theory the sequences of

SEQ ID NOs:430-437 contain the heptad repeats of the F proteins of different strains of human metapneumoviruses.

In certain embodiments, an antibody to be used with the methods of the invention binds to a heptad repeat. In certain, more specific embodiments, an antibody to be used with the methods of the invention binds to a heptad repeat of the F protein of a mammalian metapneumovirus (*e.g.*, hMPV). In certain, even more specific embodiments, an antibody to be used with the methods of the invention binds to heptad repeat 1 or heptad repeat 2 of the F protein of a mammalian metapneumovirus (*e.g.*, hMPV). In certain embodiments, an antibody to be used with the methods of the invention binds to a heptad repeat of the F protein of APV.

Alignment of the human metapneumoviral F protein with the F protein of an avian pneumovirus isolated from Mallard Duck shows 85.6% identity in the ectodomain. Alignment of the human metapneumoviral F protein with the F protein of an avian pneumovirus isolated from Turkey (subgroup B) shows 75% identity in the ectodomain. See, *e.g.*, co-owned and co-pending Provisional Application No.: 60/358,934, entitled "Recombinant Parainfluenza Virus Expression Systems and Vaccines Comprising Heterologous Antigens Derived from Metapneumovirus", filed on February 21, 2002, by Haller and Tang, which is incorporated herein by reference in its entirety. Therefore, an antigen from avian metapneumovirus, and in particular the F protein from turkey metapneumovirus is a useful antigen for generating antibodies against human metapneumovirus.

In certain embodiments, the anti-hMPV-antigen antibody is a bispecific antibody. In certain embodiments, the bispecific antibody binds to two different epitopes of the same hMPV antigen. In certain other embodiments, the bispecific antibody binds to epitopes on two different hMPV antigens. In certain embodiments, the bispecific antibody binds immunospecifically to (i) a hMPV antigen and (ii) to an APV, a PIV, and/or a RSV antigen.

In certain embodiments, an antibody to be used with the methods of the invention is a bispecific antibody that binds to the F protein of RSV and to the F protein of hMPV. The bispecific antibody can be generated by chemical procedure or a recombinant approach. The antibody can be diabody, $F(ab')_2$, $F(ab')_2$ fused with lucine zippers, single chain diabodies, etc. The antibody can also be a multivalent antibody, such as quadruplebody. In certain embodiments, a bispecific antibody is constructed using Numax or Synagis for the part of the

antibody that binds the RSV F protein in combination with an antibody that binds the hMPV F protein.

4.1.7.3 Multiple Protein Monoclonal Antibodies

To generate multiple protein monoclonal antibodies, Balb/c or SJL mice (mice can be obtained, *e.g.*, from The Jackson Laboratory, Maine) are immunized first with live hMPV and later with adjuvanted hMPV, bovine PIV or purified F protein of hMPV. In a more specific embodiment, mice are immunized intranasally one to two times with hMPV followed by intraperitoneal injections with either hMPV (to produce all types of neutralizing antibodies, *e.g.*, F or G protein) or with intranasal immunization with bPIV/hMPV F or intraperitoneal immunization of purified F protein. bPIV/hMPV F is a chimeric virus wherein the coding sequence for the hMPV F protein is inserted into bovine PIV. A more detailed description of PIV vectors and their use as expression systems can be found in co-owned and co-pending U.S. Application Nos.: 10/371,264 and 10/373,567, both filed on February 21, 2003, both of which are incorporated herein by reference in their entireties. In certain specific embodiments, for each immunization 100 microliter of virus at 10^6-10^7 pfu/ml per mouse are used.

4.1.8 ANTI-PIV-ANTIGEN ANTIBODIES

In certain embodiments, an anti-PIV-antigen antibody binds immunospecifically to a PIV nucleocapsid structural protein, a PIV fusion glycoprotein, a PIV phosphoprotein, a PIV L protein, a PIV matrix protein, a PIV HN glycoprotein, a PIV RNA-dependent RNA polymerase, a PIV Y1 protein, a PIV D protein, a F glycoprotein, a PIV hemagglutinin-neuraminidase, or a PIV C protein.

In certain embodiments, the anti-PIV-antigen antibody binds to an antigen of PIV type 1, PIV type 2, and/or PIV type 3, or any combination thereof.

In certain embodiments, an anti-PIV-antigen antibody binds to allelic variants of a PIV nucleocapsid structural protein, a PIV fusion glycoprotein, a PIV phosphoprotein, a PIV L protein, a PIV matrix protein, a PIV HN glycoprotein, a PIV RNA-dependent RNA polymerase, a PIV Y1 protein, a PIV D protein, a F glycoprotein, a PIV hemagglutinin-neuraminidase, or a PIV C protein.

In certain embodiments, the anti-PIV-antigen antibody binds immunospecifically to a PIV RNA polymerase alpha subunit (Nucleocapsid phosphoprotein), *e.g.*, having an amino

acid sequence of SEQ ID NO:407; a PIV L polymerase protein, *e.g.*, having an amino acid sequence of SEQ ID NO:408; a PIV HN glycoprotein, *e.g.*, having an amino acid sequence of SEQ ID NO:409; a PIV matrix protein, *e.g.*, having an amino acid sequence of SEQ ID NO:410; a PIV Y1 protein, *e.g.*, having an amino acid sequence of SEQ ID NO:411; a PIV C protein, *e.g.*, having an amino acid sequence of SEQ ID NO:412; a PIV phosphoprotein, *e.g.*, having an amino acid sequence of SEQ ID NO:413; a PIV nucleoprotein, *e.g.*, having an amino acid sequence of SEQ ID NO:414; a PIV F glycoprotein, *e.g.*, having an amino acid sequence of SEQ ID NO:415; a PIV D protein, *e.g.*, having an amino acid sequence of SEQ ID NO:416; a PIV hemagglutinin-neuraminidase, *e.g.*, having an amino acid sequence of SEQ ID NO:417; a PIV nucleocapsid protein, *e.g.*, having an amino acid sequence of SEQ ID NO:418; a PIV P protein, *e.g.*, having an amino acid sequence of SEQ ID NO:419.

In certain embodiments, the anti-PIV-antigen antibody binds immunospecifically to a protein/polypeptide that consists of an amino acid sequence that is at least 60%, 70%, 80%, 90%, 95%, or at least 98% identical to the amino acid sequence of an RNA polymerase alpha subunit (Nucleocapsid phosphoprotein) SEQ ID NO:407; L polymerase protein SEQ ID NO:408; HN glycoprotein SEQ ID NO:409; matrix protein SEQ ID NO:410; Y1 protein SEQ ID NO:411; C protein SEQ ID NO:412; phosphoprotein SEQ ID NO:413; nucleoprotein SEQ ID NO:414; F glycoprotein SEQ ID NO:415; D protein SEQ ID NO:416; hemagglutinin-neuraminidase SEQ ID NO:417; nucleocapsid protein SEQ ID NO:418; P protein SEQ ID NO:419. In certain embodiments, the anti-PIV-antigen antibody binds immunospecifically to a protein/polypeptide that consists of an amino acid sequence that is at most 70%, 80%, 90%, 95%, 98% or at most 100% identical to the amino acid sequence of an RNA polymerase alpha subunit (Nucleocapsid phosphoprotein) SEQ ID NO:407; L polymerase protein SEQ ID NO:408; HN glycoprotein SEQ ID NO:409; matrix protein SEQ ID NO:410; Y1 protein SEQ ID NO:411; C protein SEQ ID NO:412; phosphoprotein SEQ ID NO:413; nucleoprotein SEQ ID NO:414; F glycoprotein SEQ ID NO:415; D protein SEQ ID NO:416; hemagglutinin-neuraminidase SEQ ID NO:417; nucleocapsid protein SEQ ID NO:418; P protein SEQ ID NO:419.

4.2 PROPHYLAXIS AND THERAPY OF RESPIRATORY VIRAL INFECTIONS

The invention provides methods for broad-spectrum treatment and prevention of respiratory viral infections. To obtain broad-spectrum protection against respiratory viral infection in a subject, a plurality of antibodies, each of which can bind immunospecifically to

an epitope on a different virus that causes respiratory infections, is administered to the subject. In certain embodiments, a plurality of antibodies that bind immunospecifically to antigens of different viruses that cause respiratory infections is administered. In certain embodiments, a plurality of antibodies that bind immunospecifically to different antigens of hMPV, PIV, and/or RSV, is administered. In certain embodiments, antibodies that cross-react with antigens from different respiratory viruses are administered. In specific embodiments, an antibody that immunospecifically binds to an antigen of hMPV cross reacts with an antigen of APV, particularly turkey APV. More specifically, an antibody that binds immunospecifically to the F protein of hMPV cross-reacts with the F protein of APV.

In certain embodiments, at least one of the antibodies to be administered to a subject is an antibody-conjugate.

Administering different antibodies with different immunospecificities ensures that the prophylaxis/therapy is effective against respiratory viruses even if some antigens of the viruses have modified amino acid sequences. In general there are two approaches to ensure that at least one of the administered plurality of antibodies binds immunospecifically to one or more of the infectious respiratory viral particles. First, antibodies against different epitopes of one or more viruses may be included in the plurality of antibodies. Thus, even if one of the epitopes of the infectious respiratory viral particle is different from the corresponding epitope against which one of the antibodies was raised, another antibody of the plurality of antibodies binds immunospecifically to an epitope of the infectious respiratory viral particle. In certain embodiments, even if one of the antigens of the infectious respiratory viral particle is different from the corresponding antigen against which one of the antibodies of the plurality of antibodies was raised, another antibody of the plurality of antibodies binds immunospecifically to an antigen of the infectious respiratory viral particle. Secondly, antibodies that cross-react with different antigens from different viruses, such as the F protein from RSV and the F protein from hMPV can be included in the plurality of antibodies to broaden the spectrum of viruses, subtypes of viruses, subgroups of viruses, mutated viruses, groups of viruses, and types of viruses against which the plurality of antibodies is effective.

In certain embodiment of the invention, the antibodies that are administered to the subject have a synergistic effect in treating and/or preventing an respiratory viral infection. In certain embodiments, the combination of a variety of antibodies is effective in treating or

preventing a respiratory viral infection while the individual administration of only one antibody is not effective in treating or preventing a respiratory viral infection.

In certain embodiments, the methods of the invention include administering (i) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof; (ii) one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof; and/or (iii) one or more anti-PIV-antigen antibodies or antigen-binding fragmens thereof; and (iv) and one or more vaccines directed against viruses that cause respiratory infections. In a specific embodiment, the vaccine is directed against hMPV. Such vaccines are described in U.S. Provisional Application No.: 60/358,934, entitled "Recombinant Parainfluenza Virus Expression Systems and Vaccines Comprising Heterologous Antigens Derived from Metapneumovirus", filed February 21, 2002, which is incorporated by reference in its entirety herein.

In certain other embodiments, the methods further include administering an anti-viral agent. Anti-viral agents include, but are not limited to, nucleoside analogs, such as zidovudine, acyclovir, gangcyclovir, vidarabine, idoxuridine, trifluridine, and ribavirin, as well as foscarnet, amantadine, rimantadine, saquinavir, indinavir, ritonavir, and the alpha-interferons.

4.2.1 COMBINATION PROPHYLAXIS AND THERAPY WITH ANTI-RSV-ANTIGEN ANTIBODIES, ANTI-HMPV-ANTIGEN ANTIBODIES, AND ANTI-PIV-ANTIGEN ANTIBODIES

In certain embodiments, the invention provides methods for preventing, treating and/or ameliorating one or more symptoms of a respiratory viral infection in a subject, the method comprising administering to the subject one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof, and one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. In specific embodiments, the invention provides administering to a subject a prophylactically effective amount of one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, a prophylactically effective amount of one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof, and a prophylactically effective amount of one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof to prevent a respiratory viral infection in a subject. In specific embodiments, the invention provides administering to a subject a therapeutically effective amount of one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, a therapeutically effective amount of one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof, and a therapeutically effective amount of one or more anti-hMPV-antigen antibodies or antigen-

binding fragments thereof to treat a respiratory viral infection in a subject. In specific emodiments of the invention, the respiratory viral infection is an infection with RSV, PIV, and/or hMPV. In certain embodiments, the subject is exposed to a risk of infection with RSV, PIV, and/or hMPV.

In certain embodiments, the invention provides methods of passive immunotherapy, wherein the methods comprises administering a first dose of one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, a second dose of one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof, and a third dose of one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof and wherein the first dose reduces the incidence of a RSV infection by at least 25%, wherein the second dose reduces the incidence of a PIV infection by at least 25%, and wherein the third dose reduces the incidence of a hMPV infection by at least 25%. In certain embodiments, the first dose reduces the incidence of a RSV infection by at least 10%, 15%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 95%, or by at least 98%, wherein the second dose reduces the incidence of a PIV infection by at least 10%, 15%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 95%, or by at least 98%, and wherein the third dose reduces the incidence of a hMPV infection by at least 10%, 15%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 95%, or by at least 98%.

In certain embodiments, the invention provides a method of passive immunotherapy wherein the method comprises administering to a subject: (i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein said one or more first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; (ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein said one or more second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen, and (iii) a third dose of one or more third antibodies wherein the one or more third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen, wherein the serum titer of said one or more first antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more first antibodies or antigen-binding fragments thereof, wherein the serum titer of said one or more second antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering said one or more second antibodies or antigen-binding fragments thereof, and wherein the serum titer of said one or more third antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of

administering said one or more second antibodies or antigen-binding fragments thereof. In certain embodiments, the serum titer of said one or more first antibodies or antigen-binding fragments thereof in the subject is at least 0.1 μg/ml, 0.5 μg/ml, 1 μg/ml, 5 μg/ml, 10 μg/ml, 20 μg/ml, 30 μg/ml, 40 μg/ml, 50 μg/ml, 75 μg/ml, 100 μg/ml, 150 μg/ml, 250 μg/ml, or at least 500 μg/ml after 15 days of administering said one or more first antibodies or antigen-binding fragments thereof, wherein the serum titer of said one or more second antibodies or antigen-binding fragments thereof in the subject is at least 0.1 μg/ml, 0.5 μg/ml, 1 μg/ml, 5 μg/ml, 10 μg/ml, 20 μg/ml, 30 μg/ml, 40 μg/ml, 50 μg/ml, 75 μg/ml, 100 μg/ml, 150 μg/ml, 250 μg/ml, or at least 500 μg/ml after 15 days of administering said one or more second antibodies or antigen-binding fragments thereof, and wherein the serum titer of said one or more third antibodies or antigen-binding fragments thereof in the subject is at least 0.1 μg/ml, 0.5 μg/ml, 1 μg/ml, 5 μg/ml, 10 μg/ml, 20 μg/ml, 30 μg/ml, 40 μg/ml, 50 μg/ml, 75 μg/ml, 100 μg/ml, 150 μg/ml, 250 μg/ml, or at least 500 μg/ml after 15 days of administering said one or more second antibodies or antigen-binding fragments thereof.

In certain embodiments, the one or more anti-RSV-antigen antibodies, the one or more anti-PIV-antigen antibodies, and the one or more anti-hMPV-antigen antibodies, or any combination of these antibodies, are administered concurrently. In certain, more specific embodiments, the antibodies are administered concurrently via the same route, *e.g.*, but not limited to, intravenous or intramuscular. In certain other embodiments, the antibodies are administered concurrently via different routes.

In other embodiments, the one or more anti-RSV-antigen antibodies, the one or more anti-PIV-antigen antibodies, and the one or more anti-hMPV-antigen antibodies are administered subsequent to each other separated by a time period. In certain embodiments, the time period is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months. In a specific embodiment of the invention, the one or more anti-RSV-antigen antibodies are administered first, the one or more anti-PIV-antigen antibodies are administered second, and the one or more anti-hMPV-antigen antibodies are administered third. In a specific embodiment of the invention, the one or more anti-hMPV-antigen antibodies are administered first, the one or more anti-RSV-antigen antibodies are administered second, and the one or more anti-PIV-antigen antibodies are administered third. In a specific embodiment of the invention, the one or more anti-PIV-antigen antibodies are administered first, the one or more anti-hMPV-antigen antibodies are administered second, and the one or more anti-RSV-antigen antibodies are administered third. In certain

embodiments, at least one of the antibodies is administered in a sequence of several administrations separated by a time period. Any other order of administration is also encompassed by the methods of the present invention.

The one or more anti-PIV-antigen antibodies, the one or more anti-hMPV-antigen antibodies, and the one or more anti-RSV-antigen antibodies can also be cyclically administered. Cycling therapy involves the administration of a first prophylactic or therapeutic agent for a period of time, followed by the administration of a second prophylactic or therapeutic agent for a period of time, followed by the administration of a third prophylactic or therapeutic agent for a period of time and so forth, and repeating this sequential administration, *i.e.*, the cycle, in order to reduce the development of resistance to one of the agents, to avoid or reduce the side effects of one of the agents, and/or to improve the efficacy of the treatment.

In certain embodiments, administration of the same antibody may be repeated and the administrations may be separated by at least 10 days, 15 days, 30 days, 2 months, 3 months, or at least 6 months. In certain embodiments, administration of the same antibody may be repeated and the administrations may be separated by at most 10 days, 15 days, 30 days, 2 months, 3 months, or at least 6 months.

4.2.2 COMBINATION PROPHYLAXIS AND THERAPY WITH ANTI-RSV-ANTIGEN ANTIBODIES AND ANTI-HMPV-ANTIGEN ANTIBODIES

The present invention provides methods of preventing and/or treating and ameliorating one or more symptoms associated with a respiratory viral infection in a subject comprising administering to said subject (i) one or more first antibodies or antigen-binding fragments thereof which immunospecifically bind to one or more RSV antigens; and (ii) one or more second antibodies or antigen-binding fragments thereof which immunospecifically bind to one or more hMPV antigens. In a specific embodiment, the subject is a human. In a specific embodiment, the subject has a viral respiratory infection, in particular, is infected with RSV and/or hMPV. In a specific embodiment, the method prevents a subject from infection with RSV and/or hMPV. In a specific embodiment, the subject is susceptible to RSV and/or hMPV infection. In a specific embodiment, the subject is exposed to the risk of infection with RSV and/or hMPV infection.

In certain embodiments, the one or more first antibodies neutralize RSV. In certain embodiments, the one or more first antibodies neutralize at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least

70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% of the RSV in an *in vitro* microneutralization assay (see below). In certain embodiments, the one or more first antibodies neutralize at least 25%, at most 30%, at most 35%, at most 40%, at most 45%, at most 50%, at most 55%, at most 60%, at most 65%, at most 70%, at most 75%, at most 80%, at most 85%, at most 90%, at most 95%, at most 98% or at most 99% of the RSV in an *in vitro* microneutralization assay (as described in section 4.8.4).

In certain embodiments, the one or more second antibodies neutralize hMPV. In certain embodiments, the one or more second antibodies neutralize at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% of the hMPV in an *in vitro* microneutralization assay (see below). In certain embodiments, the one or more first antibodies neutralize at least 25%, at most 30%, at most 35%, at most 40%, at most 45%, at most 50%, at most 55%, at most 60%, at most 65%, at most 70%, at most 75%, at most 80%, at most 85%, at most 90%, at most 95%, at most 98% or at most 99% of the hMPV in an *in vitro* microneutralization assay.

In certain embodiments, at least one of the one or more antibodies that bind immunospecifically to a RSV antigen is a high affinity and/or high avidity antibody and/or has a longer serum half-life. In certain embodiments, at least one of the one or more antibodies that bind immunospecifically to a hMPV antigen is a high affinity and/or high avidity antibody and/or has a longer serum half-life.

The high affinity and/or high avidity of the antibodies of the invention enable the use of lower doses of the antibodies compared to non-high affinity or non-high avidity for the amelioration of symptoms associated with RSV infection and/or hMPV infection. The use of lower doses of antibodies which immunospecifically bind to one or more RSV antigens and the use of lower doses of antibodies which immunospecifically bind to one or more hMPV antigens reduces the likelihood of adverse effects, as well as providing a more effective prophylaxis. Further, high affinity and/or high avidity of the antibodies enable less frequent administration of said antibodies than previously thought to be necessary for the prevention, neutralization, treatment and the amelioration of symptoms associated with RSV infection and hMPV infection, respecively.

In certain embodiments, the one or more antibodies that bind immunospecifically to a RSV antigen and/or the one or more antibodies that bind immunospecifically to a hMPV

antigen can be administered directly to the site of RSV infection. In particular, at least one of the antibodies can be administered by pulmonary delivery. Such a mode of administration can reduce the dosage and frequency of administration of the antibodies to a subject.

In certain embodiments, the serum titer of at least one of the administered antibodies is 1 μg/ml or less, 2 μg/ml or less, 5 μg/ml or less, 6 μg/ml or less, 10 μg/ml or less, 15 μg/ml or less, 20 μg/ml or less, or 25 μg/ml or less. In certain embodiments, the serum titer of at least one of the administered antibodies is at least 1 μg/ml, at least 2 μg/ml, at least 5 μg/ml, at least 6 μg/ml, at least 10 μg/ml, at least 15 μg/ml, at least 20 μg/ml, at least 25 μg/ml, at least 50 μg/ml, at least 100 μg/ml, at least 125 μg/ml, at least 150 μg/ml, at least 175 μg/ml, at least 200 μg/ml, at least 225 μg/ml, at least 250 μg/ml, at least 275 μg/ml, at least 300 μg/ml, at least 325 μg/ml, at least 350 μg/ml, at least 375 μg/ml, or at least 400 μg/ml. Preferably a serum titer or serum titer of 1 μg/ml or less, 2 μg/ml or less, 5 μg/ml or less, 6 μg/ml or less, 10 μg/ml or less, 15 μg/ml or less, 20 μg/ml or less, or 25 μg/ml or less is achieved approximately 20 days (preferably 25, 30, 35 or 40 days) after administration of a first dose of antibodies or antigen-binding fragments thereof which immunospecifically bind to a RSV antigen and/or to a hMPV antigen and without administration of any other doses of said antibodies or antigen-binding fragments thereof. Preferably a serum titer or serum titer of at least 1 μg/ml, at least 2 μg/ml, at least 5 μg/ml, at least 6 μg/ml, at least 10 μg/ml, at least 15 μg/ml, at least 20 μg/ml, at least 25 μg/ml, at least 50 μg/ml, at least 100 μg/ml, at least 125 μg/ml, at least 150 μg/ml, at least 175 μg/ml, at least 200 μg/ml, at least 225 μg/ml, at least 250 μg/ml, at least 275 μg/ml, at least 300 μg/ml, at least 325 μg/ml, at least 350 μg/ml, at least 375 μg/ml, or at least 400 μg/ml is achieved approximately 20 days (preferably 25, 30, 35 or 40 days) after administration of a first dose of antibodies or antigen-binding fragments thereof which immunospecifically bind to a RSV antigen and/or to a hMPV antigen and without administration of any other doses of said antibodies or antigen-binding fragments thereof.

In specific embodiments, a serum titer in a non-primate mammal of at least 0.4 μg/ml, 1 μg/ml, 4 μg/ml, 10 μg/ml, 40 μg/ml, at least 80 μg/ml, at least 100 μg/ml, at least 120 μg/ml, at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, or at least 300 μg/ml, of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to a RSV antigen and/or of one or more antibodies or antigen-binding fragments thereof that bind immunospecifically to a hMPV antigen is achieved at least 1 day after administering a dose of less than 20 mg/kg, 15 mg/kg, 10 mg/kg, less than 2.5 mg/kg, less than 1 mg/kg, or less

than 0.5 mg/kg of the antibodies or antibody fragments to the non-primate mammal. In another embodiment, a serum titer in a non-primate mammal of at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, at least 300 μg/ml, at least 350 μg/ml, or at least 400 μg/ml of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens and/or that bind immunospecifically to a hMPV antigen is achieved at least 1 day after administering a dose of approximately 5 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, or 30 mg/kg of the antibodies or antibody fragments to the non-primate mammal.

In another embodiment, a serum titer in a primate of at least 0.4 μg/ml, 1 μg/ml, 10 μg/ml, 40 μg/ml, preferably at least 80 μg/ml, at least 100 μg/ml, at least 120 μg/ml, at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, or at least 300 μg/ml of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens and/or to one or more hMPV antigens is achieved at least 30 days after administering a first dose of less than 5 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, or 30 mg/kg , preferably less than 3 mg/kg, less than 1 mg/kg, or less than 0.5 mg/kg of the antibodies or antigen-binding fragments thereof to the primate. In yet another embodiment, a serum titer in a primate of at least 200 μg/ml, at least 250 μg/ml, at least 300 μg/ml, at least 350 μg/ml, or at least 400 μg/ml of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens and/or one or more hMPV antigens is achieved at least 30 days after administering a first dose of approximately 5 mg/kg, 10 mg/kg, 15 mg/kg, 20 mg/kg, 25 mg/kg, or 30 mg/kg of the antibodies or antigen-binding fragments thereof to the primate. In accordance with these embodiments, the primate is preferably a human.

The present invention provides methods for preventing, treating, or ameliorating one or more symptoms associated with a respiratory viral infection in a mammal, preferably a human, said methods comprising administering a first dose to said mammal of (i) a prophylactically or therapeutically effective amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens, and (ii) a prophylactically or therapeutically effective amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more hMPV antigens, wherein said effective amount is less than 1.5 mg/kg, 8 mg/kg, 15 mg/kg, 50 mg/kg, or less than 100 mg/kg or approximately this amount of said antibodies or antigen-binding fragments thereof and which results in a serum titer of greater than 40 μg/ml 30 days after the

first administration and prior to any subsequent administration. In one embodiment, the respiratory viral infection in a human subject is prevented or treated, or one or more symptoms associated with the respiratory viral infection is ameliorated by administering (i) a first dose of less than 20 mg/kg, 15 mg/kg, 10 mg/kg, preferably less than 5 mg/kg, less than 3 mg/kg, or less than 1 mg/kg or approximately this amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens; and (ii) a second dose of less than 20 mg/kg, 15 mg/kg, 10 mg/kg, less than 5 mg/kg, less than 3 mg/kg, or less than 1 mg/kg or approximately this amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more hMPV antigens so that a serum antibody titer of at least 40 μg/ml, at least 80 μg/ml, or at least 120 μg/ml, at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, or at least 300 μg/ml is achieved 30 days after the administration of the first dose of the antibodies or antibody fragments and prior to the administration of a subsequent dose. In another embodiment, a respiratory infection in a human subject is prevented or treated, or one or more symptoms associated with a respiratory viral infection is ameliorated by administering a first dose of approximately 15 mg/kg of (i) one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens; and (ii) one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens so that a serum antibody titer of at least 10 μg/ml, 25 μg/ml, 50 μg/ml, 75 μg/ml, or at least 100 μg/ml, at least 200 μg/ml, at least 250 μg/ml, at least 300 μg/ml, at least 350 μg/ml, or at least 400 μg/ml is achieved 30 days after the administration of the first dose of the antibodies or antibody fragments and prior to the administration of a subsequent dose.

In certain embodiments, the respiratory viral infection is an infection with RSV and/or hMPV.

In certain embodiments of the invention, the fragments of the antibodies, *i.e.*, the one or more antibodies that bind immunospecifically to a RSV antigen and/or the one or more antibodies that bind immunospecifically to a hMPV antigen comprise a variable heavy ("VH") domain.

In certain embodiments of the invention, the fragments of the one or more antibodies that bind immunospecifically to a RSV antigen and/or the fragments of the one or more antibodies that bind immunospecifically to a hMPV antigen comprise a variable light ("VL").

In certain embodiments, at least one of the fragments or the antibodies comprises a VH domain and a VL domain.

In certain embodiments of the invention, the antibodies are administered via sustained release formulations.

In certain embodiments the one or more antibodies or antigen-binding fragments thereof that bind immunospecifically to one or more RSV antigens (hereafter "anti-RSV-antigen antibodies or antigen-binding fragments thereof") and the one or more antibodies that bind immunospecifically to one or more hMPV antigens (hereafter "anti-hMPV-antigen antibodies or antigen-binding fragments thereof") are administered concurrently. In certain, more specific embodiments, the antibodies are administered concurrently via the same route, *e.g.*, but not limited to, intravenous or intramuscular. In certain other embodiments, the antibodies are administered concurrently via different routes.

In certain other embodiments, the anti-RSV-antigen antibodies or antigen-binding fragments thereof are administered prior to the administration of the anti-hMPV-antigen antibodies or antigen-binding fragments thereof. In certain other embodiments, the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered prior to the administration of the anti-RSV-antigen antibodies or antigen-binding fragments thereof.

In certain embodiments, the anti-RSV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of individual administrations separated by a time period and the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered prior to, concurrently with, or subsequent to the sequence of administering the anti-RSV-antigen antibodies. In certain embodiments, the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of individual administrations separated by a time period and the anti-RSV-antigen antibodies or antigen-binding fragments thereof are administered prior to, concurrently with, or subsequent to the sequence of administering the anti-hMPV-antigen antibodies. In certain embodiments, the time period is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

In certain embodiments, both the anti-RSV-antigen antibodies or antigen-binding fragments thereof and the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of individual administrations separated by a time period. In certain more specific embodiments, the two sequences of administrations are in phase with each other. In other embodiments, the two sequences are out-of-phase with each other.

The present invention provides compositions comprising (i) one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more RSV antigens, and (ii) one or more antibodies or antigen-binding fragments thereof that bind immunospecifically to one or more hMPV antigen. In certain embodiments, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

In certain embodiments, administration of the same antibody may be repeated and the administrations may be separated by at least 10 days, 15 days, 30 days, 2 months, 3 months, or at least 6 months. In certain embodiments, administration of the same antibody may be repeated and the administrations may be separated by at most 10 days, 15 days, 30 days, 2 months, 3 months, or at least 6 months.

4.2.3 COMBINATION PROPHYLAXIS AND THERAPY OF ANTI-PIV-ANTIGEN ANTIBODIES AND ANTI-HMPV-ANTIGEN ANTIBODIES

The present invention provides methods of preventing and/or treating and ameliorating one or more symptoms associated with a respiratory viral infection in a subject comprising administering to said subject (i) one or more first antibodies or antigen-binding fragments thereof which immunospecifically bind to one or more PIV antigens; and (ii) one or more second antibodies or antigen-binding fragments thereof which immunospecifically bind to one or more hMPV antigens. In a specific embodiment, the subject is a human infected with PIV and hMPV. In a specific embodiment, the method prevents a subject from infection with PIV and hMPV. In a specific embodiment, the subject is susceptible to PIV and hMPV infection.

In certain embodiments, the one or more first antibodies neutralize PIV. In certain embodiments, the one or more first antibodies neutralize at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% of the PIV in an *in vitro* microneutralization assay (see below). In certain embodiments, the one or more first antibodies neutralize at least 25%, at most 30%, at most 35%, at most 40%, at most 45%, at most 50%, at most 55%, at most 60%, at most 65%, at most 70%, at most 75%, at most 80%, at most 85%, at most 90%, at most 95%, at most 98% or at most 99% of the PIV in an *in vitro* microneutralization assay (as described in section 4.8.4).

In certain embodiments, the one or more second antibodies neutralize hMPV. In certain embodiments, the one or more second antibodies neutralize at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% of the hMPV in an *in vitro* microneutralization assay (see below). In certain embodiments, the one or more first antibodies neutralize at least 25%, at most 30%, at most 35%, at most 40%, at most 45%, at most 50%, at most 55%, at most 60%, at most 65%, at most 70%, at most 75%, at most 80%, at most 85%, at most 90%, at most 95%, at most 98% or at most 99% of the hMPV in an *in vitro* microneutralization assay.

In certain embodiments, at least one of the one or more antibodies that bind immunospecifically to a PIV antigen is a high affinity and/or high avidity antibody and/or has a longer serum half-life. In certain embodiments, at least one of the one or more antibodies that bind immunospecifically to a hMPV antigen is a high affinity and/or high avidity antibody and/or has a longer serum half-life.

The high affinity and/or high avidity of the antibodies of the invention enable the use of lower doses of the antibodies compared to non-high affinity or non-high avidity for the amelioration of symptoms associated with PIV infection and/or hMPV infection. The use of lower doses of antibodies which immunospecifically bind to one or more PIV antigens and the use of lower doses of antibodies which immunospecifically bind to one or more hMPV antigens reduces the likelihood of adverse effects, as well as providing a more effective prophylaxis. Further, high affinity and/or high avidity of the antibodies enable less frequent administration of said antibodies than previously thought to be necessary for the prevention, neutralization, treatment and the amelioration of symptoms associated with PIV infection and hMPV infection, respectively.

In certain embodiments, the one or more antibodies that bind immunospecifically to a PIV antigen and/or the one or more antibodies that bind immunospecifically to a hMPV antigen can be administered directly to the site of PIV infection. In particular, at least one of the antibodies can be administered by pulmonary delivery. Such a mode of administration can reduce the dosage and frequency of administration of the antibodies to a subject.

In certain embodiments, the serum titer of at least one of the administered antibodies is 1 μg/ml or less, 2 μg/ml or less, 5 μg/ml or less, 6 μg/ml or less, 10 μg/ml or less, 15 μg/ml or less, 20 μg/ml or less, 25 μg/ml or less, 100 μg/ml or less, or 250 μg/ml or less. In certain embodiments, the serum titer of at least one of the administered antibodies is at least 1 μg/ml,

at least 2 μg/ml, at least 5 μg/ml, at least 6 μg/ml, at least 10 μg/ml, at least 15 μg/ml, at least 20 μg/ml, at least 25 μg/ml, at least 50 μg/ml, at least 100 μg/ml, at least 125 μg/ml, at least 150 μg/ml, at least 175 μg/ml, at least 200 μg/ml, at least 225 μg/ml, at least 250 μg/ml, at least 275 μg/ml, at least 300 μg/ml, at least 325 μg/ml, at least 350 μg/ml, at least 375 μg/ml, or at least 400 μg/ml. Preferably a serum titer or serum titer of 1 μg/ml or less, 2 μg/ml or less, 5 μg/ml or less, 6 μg/ml or less, 10 μg/ml or less, 15 μg/ml or less, 20 μg/ml or less, or 25 μg/ml or less is achieved approximately 20 days (preferably 25, 30, 35 or 40 days) after administration of a first dose of antibodies or antigen-binding fragments thereof which immunospecifically bind to a PIV antigen and/or to a hMPV antigen and without administration of any other doses of said antibodies or antigen-binding fragments thereof. Preferably a serum titer or serum titer of at least 1 μg/ml, at least 2 μg/ml, at least 5 μg/ml, at least 6 μg/ml, at least 10 μg/ml, at least 15 μg/ml, at least 20 μg/ml, at least 25 μg/ml, at least 50 μg/ml, at least 100 μg/ml, at least 125 μg/ml, at least 150 μg/ml, at least 175 μg/ml, at least 200 μg/ml, at least 225 μg/ml, at least 250 μg/ml, at least 275 μg/ml, at least 300 μg/ml, at least 325 μg/ml, at least 350 μg/ml, at least 375 μg/ml, or at least 400 μg/ml is achieved approximately 20 days (preferably 25, 30, 35 or 40 days) after administration of a first dose of antibodies or antigen-binding fragments thereof which immunospecifically bind to a PIV antigen and/or to a hMPV antigen and without administration of any other doses of said antibodies or antigen-binding fragments thereof.

In specific embodiments, a serum titer in a non-primate mammal of at least 0.4 μg/ml, 1 μg/ml, 4 μg/ml, 10 μg/ml, 40 μg/ml, at least 80 μg/ml, at least 100 μg/ml, at least 120 μg/ml, at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, or at least 300 μg/ml, of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to a PIV antigen and/or of one or more antibodies or antigen-binding fragments thereof that bind immunospecifically to a hMPV antigen is achieved at least 1 day after administering a dose of less than 100 mg/kg, 50 mg/kg, 10 mg/kg, less than 2.5 mg/kg, less than 1 mg/kg, or less than 0.5 mg/kg of the antibodies or antibody fragments to the non-primate mammal. In another embodiment, a serum titer in a non-primate mammal of at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, at least 300 μg/ml, at least 350 μg/ml, or at least 400 μg/ml of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens and/or that bind immunospecifically to a hMPV antigen is achieved at least 1 day after administering a dose of approximately 5 mg/kg of the antibodies or antibody fragments to the non-primate mammal.

In another embodiment, a serum titer in a primate of at least 0.4 μg/ml, 1 μg/ml, 4 μg/ml, 10 μg/ml, 40 μg/ml, preferably at least 80 μg/ml, at least 100 μg/ml, at least 120 μg/ml, at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, or at least 300 μg/ml of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens and/or to one or more hMPV antigens is achieved at least 30 days after administering a first dose of less than 5 mg/kg, preferably less than 3 mg/kg, less than 1 mg/kg, or less than 0.5 mg/kg of the antibodies or antigen-binding fragments thereof to the primate. In yet another embodiment, a serum titer in a primate of at least 200 μg/ml, at least 250 μg/ml, at least 300 μg/ml, at least 350 μg/ml, or at least 400 μg/ml of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens and/or one or more hMPV antigens is achieved at least 30 days after administering a first dose of approximately 15 mg/kg of the antibodies or antigen-binding fragments thereof to the primate. In accordance with these embodiments, the primate is preferably a human.

The present invention provides methods for preventing, treating, or ameliorating one or more symptoms associated with a respiratory viral infection in a mammal, preferably a human, said methods comprising administering a first dose to said mammal of (i) a prophylactically or therapeutically effective amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens, and (ii) a prophylactically or therapeutically effective amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more hMPV antigens, wherein said effective amount is less than 1.5 mg/kg, 15 mg/kg, 50 mg/kg, or 100 mg/kg or approximately this amount of said antibodies or antigen-binding fragments thereof and which results in a serum titer of greater than 0.4 μg/ml, 1 μg/ml, 4 μg/ml, 10 μg/ml, 40 μg/ml 30 days after the first administration and prior to any subsequent administration. In one embodiment, the respiratory viral infection in a human subject is prevented or treated, or one or more symptoms associated with the respiratory viral infection is ameliorated by administering (i) a first dose of less than 100 mg/kg or less than10 mg/kg, about 15 mg/kg less than 5 mg/kg, less than 3 mg/kg, or less than 1 mg/kg or approximately this amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens; and (ii) a first dose of less than 10 mg/kg, about 15 mg/kg less than 5 mg/kg, less than 3 mg/kg, or less than 1 mg/kg or approximately this amount of one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or

more hMPV antigens so that a serum antibody titer of at least 0.4 μg/ml, 1 μg/ml, 4 μg/ml, 10 μg/ml, 40 μg/ml, preferably at least 80 μg/ml, or at least 120 μg/ml, at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, or at least 300 μg/ml is achieved 30 days after the administration of the first dose of the antibodies or antibody fragments and prior to the administration of a subsequent dose. In another embodiment, a respiratory infection in a human subject is prevented or treated, or one or more symptoms associated with a respiratory viral infection is ameliorated by administering a first dose of approximately 15 mg/kg of (i) one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens; and (ii) one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens so that a serum antibody titer of at least 1 μg/ml, 5 μg/ml, 10 μg/ml, 50 μg/ml, 75 μg/ml, or at least 100 μg/ml, at least 200 μg/ml, at least 250 μg/ml, at least 300 μg/ml, at least 350 μg/ml, or at least 400 μg/ml is achieved 30 days after the administration of the first dose of the antibodies or antibody fragments and prior to the administration of a subsequent dose.

In certain embodiments, the respiratory viral infection is an infection with PIV and hMPV.

In certain embodiments of the invention, the fragments of the antibodies, *i.e.*, the one or more antibodies that bind immunospecifically to a PIV antigen and/or the one or more antibodies that bind immunospecifically to a hMPV antigen comprise a variable heavy ("VH") domain.

In certain embodiments of the invention, the fragments of the one or more antibodies that bind immunospecifically to a PIV antigen and/or the fragments of the one or more antibodies that bind immunospecifically to a hMPV antigen comprise a variable light ("VL").

In certain embodiments, at least one of the fragments or the antibodies comprises a VH domain and a VL domain.

In certain embodiments of the invention, the antibodies are administered via sustained release formulations.

In certain embodiments the one or more antibodies or antigen-binding fragments thereof that bind immunospecifically to one or more PIV antigens (hereafter "anti-PIV-antigen antibodies or antigen-binding fragments thereof") and the one or more antibodies that bind immunospecifically to one or more hMPV antigens (hereafter "anti-hMPV-antigen antibodies or antigen-binding fragments thereof") are administered concurrently. In certain, more specific embodiments, the antibodies are administered concurrently via the same route,

e.g., but not limited to, intravenous or intramuscular. In certain other embodiments, the antibodies are administered concurrently via different routes.

In certain other embodiments, the anti-PIV-antigen antibodies or antigen-binding fragments thereof are administered prior to the administration of the anti-hMPV-antigen antibodies or antigen-binding fragments thereof. In certain other embodiments, the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered prior to the administration of the anti-PIV-antigen antibodies or antigen-binding fragments thereof.

In certain embodiments, the anti-PIV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of individual administrations separated by a time period and the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered prior to, concurrently with, or subsequent to the sequence of administering the anti-PIV-antigen antibodies. In certain embodiments, the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of individual administrations separated by a time period and the anti-PIV-antigen antibodies or antigen-binding fragments thereof are administered prior to, concurrently with, or subsequent to the sequence of administering the anti-hMPV-antigen antibodies. In certain embodiments, the time period is 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

In certain embodiments, both the anti-PIV-antigen antibodies or antigen-binding fragments thereof and the anti-hMPV-antigen antibodies or antigen-binding fragments thereof are administered in a sequence of individual administrations separated by a time period. In certain more specific embodiments, the two sequences of administrations are in phase with each other. In other embodiments, the two sequences are out-of-phase with each other.

The present invention provides compositions comprising (i) one or more antibodies or antigen-binding fragments thereof that immunospecifically bind to one or more PIV antigens, and (ii) one or more antibodies or antigen-binding fragments thereof that bind immunospecifically to one or more hMPV antigen. In certain embodiments, the pharmaceutical compositions further comprise a pharmaceutically acceptable carrier.

In certain embodiments, administration of the same antibody may be repeated and the administrations may be separated by at least 10 days, 15 days, 30 days, 2 months, 3 months, or at least 6 months. In certain embodiments, administration of the same antibody may be

repeated and the administrations may be separated by at most 10 days, 15 days, 30 days, 2 months, 3 months, or at least 6 months.

4.3 PROPHYLACTIC AND THERAPEUTIC USES OF ANTIBODIES

Antibodies to be used with the methods of the invention are anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies.

The present invention is directed to antibody-based therapies which involve administering antibodies or antigen-binding fragments thereof to a mammal, preferably a human, for preventing, treating, or ameliorating one or more symptoms associated with a RSV, PIV, and/or hMPV infection. In particular, the methods of the invention comprise (i) administering one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof; (ii) administering one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof; or (iii) administering one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof, and one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. Prophylactic and therapeutic compositions of the invention include, but are not limited to, (i) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof; (ii) one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof; or (iii) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof, and one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. Antibodies to be used with the methods of the invention or fragments thereof may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

Antibodies or antigen-binding fragments thereof which do not prevent RSV, PIV, and/or hMPV from binding its host cell receptor but inhibit or downregulate RSV, PIV, and/or hMPV replication can also be administered to a mammal to treat, prevent or ameliorate one or more symptoms associated with a respiratory infection. The ability of an antibody or fragment thereof to inhibit or downregulate RSV, PIV, and/or hMPV replication may be determined by techniques described herein or otherwise known in the art. For

example, the inhibition or downregulation of RSV, PIV, and/or hMPV replication can be determined by detecting the RSV titer in the lungs of a mammal, preferably a human.

In a specific embodiment, an antibody to be used with the methods of the invention or fragments thereof inhibit or downregulates RSV, PIV, and/or hMPV replication by at least 99%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, at least 50%, at least 45%, at least 40%, at least 45%, at least 35%, at least 30%, at least 25%, at least 20%, or at least 10% relative to RSV, PIV, and/or hMPV replication, respectively, in absence of said antibodies or antibody fragments. In another embodiment, a combination of antibodies, a combination of antibody fragments, or a combination of antibodies and antibody fragments inhibit or downregulate a RSV, PIV, and/or hMPV replication, respectively, by at least 99%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, at least 50%, at least 45%, at least 40%, at least 45%, at least 35%, at least 30%, at least 25%, at least 20%, or at least 10% relative to RSV replication in absence of said antibodies and/or antibody fragments.

One or more antibodies of the present invention or fragments thereof that immunospecifically bind to one or more RSV antigens, one or more PIV antigens, and/or one or more hMPV antigens may be used locally or systemically in the body as a therapeutic. The antibodies to be used with the methods of this invention or fragments thereof may also be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, *e.g.*, IL-2, IL-3 and IL-7), which, for example, serve to increase the number or activity of effector cells which interact with the antibodies. The antibodies to be used with the methods of this invention or fragments thereof may also be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, *e.g.*, IL-2, IL-3 and IL-7), which, for example, serve to increase the immune response. The antibodies to be used with the methods of this invention or fragments thereof may also be advantageously utilized in combination with one or more drugs used to treat RSV infection such as, for example anti-viral agents. Antibodies to be used with the methods of the invention or fragments may be used in combination with one or more of the following drugs: NIH-351 (Gemini Technologies), RSVf-2 (Intracel), F-50042 (Pierre Fabre), T-786 (Trimeris), VP-36676 (ViroPharma), RFI-641 (American Home Products), VP-14637 (ViroPharma), PFP-1 and antiviral PFP-2 (American Home Products), RSV vaccine (Avant Immunotherapeutics), and F-50077 (Pierre Fabre). In certain embodiments, antibodies to be used with the methods

of the invention or fragments may be used in combination with the high affinity human monoclonal antibodies specific to RSV F-protein as disclosed in U.S. Patent No.: 5,811,524, by Brams et al., issued September 22, 1998, which is incorporated herein by reference in its entirety.

The antibodies to be used with the methods of the invention may be administered alone or in combination with other types of treatments (*e.g.*, hormonal therapy, immunotherapy, and anti-inflammatory agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human or humanized antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

In certain embodiments, high affinity and/or potent *in vivo* inhibiting antibodies and/or neutralizing antibodies that immunospecifically bind to a RSV, PIV, and/or hMPV antigen, for both immunoassays directed to RSV, PIV, and/or hMPV, prevention of RSV, PIV, and/or hMPV infection and therapy for RSV, PIV, and/or hMPV infection are used.

In certain embodiments, the therapeutic and/or prophylactic methods of the invention are used to treat, prevent or ameliorate one or more symptoms associated with a respiratory viral infection in a human with cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency or acquired immunodeficiency, or to a human who has had a bone marrow transplant. In certain embodiments, the respiratory viral infection is an infection with RSV, PIV, and/or hMPV. In certain embodiments, the therapeutic and/or prophylactic methods of the invention are used to treat, prevent or ameliorate one or more symptoms associated with a respiratory viral infection in a human infant, preferably a human infant born prematurely or a human infant at risk of hospitalization for RSV infection to treat, prevent or ameliorate one or more symptoms associated with RSV infection. In certain embodiments, the therapeutic and/or prophylactic methods of the invention are used to treat, prevent or ameliorate one or more symptoms associated with a respiratory viral infection in the elderly or people in group homes (*e.g.*, nursing homes or rehabilitation centers).

In certain embodiments of the invention, the target population for the therapeutic methods of the invention is defined by age. In certain embodiments, the target population for the therapeutic methods of the invention is characterized by a disease or disorder in addition to a respiratory tract infection.

In a specific embodiment, the target population encompasses young children, below 2 years of age. In a more specific embodiment, the children below the age of 2 years do not suffer from illnesses other than respiratory tract infection.

In other embodiments, the target population encompasses patients above 5 years of age. In a more specific embodiment, the patients above the age of 5 years suffer from an additional disease or disorder including cystic fibrosis, leukaemia, and non-Hodgkin lymphoma, or recently received bone marrow or kidney transplantation.

In a specific embodiment of the invention, the target population encompasses subjects in which the hMPV infection is associated with immunosuppression of the hosts. In a specific embodiment, the subject is an immunocompromised individual. In a specific embodiment, a subject to be treated with the methods of the invention is also infected with HIV.

In a specific embodiments, the subject to be treated with the methods of the invention has been diagnosed with severe respiratory syncytial virus bronchilitis. Without being bound by theory, an individual diagnosed with severe respiratory syncytial virus is also likely to be infected with hMPV. In a specific embodiments, the subject to be treated with the methods of the invention has been diagnosed with acute respiratory tract illness.

In certain embodiments, the target population for the methods of the invention encompasses the elderly.

In a specific embodiment, the subject to be treated or diagnosed with the methods of the invention was infected with hMPV in the winter months.

In certain embodiments, an effective amount of the anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antibody fragments thereof reduces the RSV, PIV, and/or hMPV titers in the lung as measured, for example, by the concentration of RSV, PIV, and/or hMPV in sputum samples or a lavage from the lungs from a mammal. In certain embodiments, an effective amount of an antibody to be used with the invention is sufficient to induce an immune response in the mammal.

In certain embodiments, the antibodies to be used with the methods of the invention are administered via sustained release formulations.

In certain embodiments, an antibody to be used with the methods of the invention binds to a heptad repeat. In certain embodiments, an antibody to be used with the methods of the invention binds to a heptad repeat of RSV, PIV, or hMPV. In certain embodiments, an antibody to be used with the methods of the invention binds to a heptad repeat of the F

protein of RSV, PIV, or hMPV. In certain, more specific embodiments, an antibody to be used with the methods of the invention binds to a heptad repeat of the F protein of a mammalian metapneumovirus (*e.g.*, hMPV). In certain, even more specific embodiments, an antibody to be used with the methods of the invention binds to heptad repeat 1 or heptad repeat 2 of the F protein of a mammalian metapneumovirus (*e.g.*, hMPV).

In certain embodiments of the invention, an antibody that immunospecifically binds to an antigen of hMPV of subgroup A or subgroup B can be used with the methods of the invention. In certain embodiments of the invention, an antibody that immunospecifically binds to an antigen of hMPV of variant A1, A2, B1 or B2.

4.3.1 METHODS OF ADMINISTRATION OF ANTIBODIES

The invention provides methods of treatment, prophylaxis, and amelioration of one or more symptoms associated with respiratory viral infection by administrating to a subject of an effective amount of one or more antibodies or fragment thereof, or pharmaceutical composition comprising one or more antibodies of the invention or fragment thereof. In particular, the antibodies to be used with the methods of the invention are administered as a mixture, *e.g.*, a composition comprising anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies, or any combination thereof. In a preferred aspect, an antibody or fragment thereof is substantially purified (*i.e.*, substantially free from substances that limit its effect or produce undesired side-effects). The subject is preferably a mammal such as non-primate (*e.g.*, cows, pigs, horses, cats, dogs, rats etc.) and a primate (*e.g.*, monkey such as a cynomolgous monkey and a human). In a preferred embodiment, the subject is a human. In another preferred embodiment, the subject is a human infant or a human infant born prematurely. In more specific embodiments, the prematurely born infant was born between 30-35 weeks gestational age or between 35-40 weeks of gestational age. In a preferred embodiment, the prematurely born infant was born between 32 and 35 weeks of gestational age. In certain other embodiments, the prematurely born infant was born at less than 32 weeks gestational age. In certain other embodiments, the prematurely born infant was born at 35-38 weeks gestational age. In other embodiments, the subject is an infant born at 38-40 weeks gestational age or greater than 40 weeks gestational age. In another embodiment, the subject is a human with cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency or acquired immunodeficiency, a human who has had a bone marrow transplant, or an elderly human.

Various delivery systems are known and can be used to administer an antibody or an antigen-binding fragment thereof, *e.g.*, encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the antibody or antibody fragment, receptor-mediated endocytosis (see, *e.g.*, Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of administering an antibody or fragment thereof, or pharmaceutical composition include, but are not limited to, parenteral administration (*e.g.*, intradermal, intramuscular, intraperitoneal, intravenous and subcutaneous), epidural, and mucosal (*e.g.*, intranasal and oral routes). In a specific embodiment, antibodies or antigen-binding fragments thereof, or pharmaceutical compositions are administered intramuscularly, intravenously, or subcutaneously. The compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (*e.g.*, oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, pulmonary administration can also be employed, *e.g.*, by use of an inhaler or nebulizer, and formulation with an aerosolizing agent. See, *e.g.*, U.S. Patent Nos. 6,019,968, 5,985, 320, 5,985,309, 5,934,272, 5,874,064, 5,855,913, 5,290,540, and 4,880,078; and PCT Publication Nos. WO 92/19244, WO 97/32572, WO 97/44013, WO 98/31346, and WO 99/66903, each of which is incorporated herein by reference their entirety. In a preferred embodiment, an antibody or fragment thereof, or composition comprising the antibodies to be used with the methods of the invention using Alkermes AIR™ pulmonary drug delivery technology (Alkermes, Inc., Cambridge, MA).

In certain embodiments, an antibody or fragment thereof is packaged in a hermetically sealed container such as an ampoule or sachette indicating the quantity of antibody or antibody fragment. In one embodiment, each antibody or antibody fragment or combination thereof is supplied as a dry sterilized lyophilized powder or water free concentrate in a hermetically sealed container and can be reconstituted, *e.g.*, with water or saline to the appropriate concentration for administration to a subject. For stabilized liquid antibody formulations, see U.S. Provisional Patent Application Nos.: 60/388,920, filed on June 14, 2002, and 60/388,921, filed June 14, 2002, which are incorporated by reference herein in their entireties. Preferably, each antibody or antibody fragment or combination thereof is supplied as a dry sterile lyophilized powder in a hermetically sealed container at a unit dosage for each antibody of at least 5 mg, more preferably at least 10 mg, at least 15 mg, at

least 25 mg, at least 35 mg, at least 45 mg, at least 50 mg, or at least 75 mg. Each lyophilized antibody or antibody fragment or combination thereof should be stored at between 2 and 8°C in its original container and the antibody or antibody fragment should be administered within 12 hours, preferably within 6 hours, within 5 hours, within 3 hours, or within 1 hour after being reconstituted. In an alternative embodiment, an antibody or fragment thereof is supplied in liquid form in a hermetically sealed container indicating the quantity and concentration of the antibody or antibody fragment. Preferably, the liquid form of the antibody or fragment thereof or combination thereof is supplied in a hermetically sealed container at a concentration for each antibody least 1 mg/ml, more preferably at least 2.5 mg/ml, at least 5 mg/ml, at least 8 mg/ml, at least 10 mg/ml, at least 15 mg/ml, at least 25 mg/ml, at least 50 mg/ml, at least 100 mg/ml, at least 125 mg/ml, at least 150 mg/ml, at least 200 mg/ml, or at least 250 mg/ml, or approximately 2.5 mg/ml, 5 mg/ml, 8 mg/ml, 10 mg/ml, 15 mg/ml, 25 mg/ml, 50 mg/ml, 100 mg/ml, 125 mg/ml, 150 mg/ml, 200 mg/ml, or 250 mg/ml.

In a specific embodiment, it may be desirable to administer the antibodies locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion, by injection, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when administering a an antibody or fragment thereof, care must be taken to use materials to which the antibody or antibody fragment does not absorb. In a specific embodiment, the antibodies may be administered by pulmonary delivery.

In another embodiment, an antibody can be delivered in a vesicle, in particular a liposome (see Langer, Science 249:1527-1533 (1990); Treat *et al.*, in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353- 365 (1989); Lopez-Berestein, ibid., pp. 3 17-327; see generally ibid.).

In yet another embodiment, an antibody can be delivered in a controlled release or sustained release system. In one embodiment, a pump may be used to achieve controlled or sustained release (see Langer, supra; Sefton, 1987, CRC Crit. Ref. Biomed. Eng. 14:20; Buchwald et al., 1980, Surgery 88:507; Saudek et al., 1989, N. Engl. J. Med. 321:574). In another embodiment, polymeric materials can be used to achieve controlled or sustained release of the antibodies of the invention or fragments thereof (see *e.g.*, Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974);

Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, 1983, J., Macromol. Sci. Rev. Macromol. Chem. 23:61; see also Levy et al., 1985, Science 228:190; During et al., 1989, Ann. Neurol. 25:351; Howard et al., 1989, J. Neurosurg. 7 1:105); U.S. Patent No. 5,679,377; U.S. Patent No. 5,916,597; U.S. Patent No. 5,912,015; U.S. Patent No. 5,989,463; U.S. Patent No. 5,128,326; PCT Publication No. WO 99/15154; and PCT Publication No. WO 99/20253. Examples of polymers used in sustained release formulations include, but are not limited to, poly(2-hydroxy ethyl methacrylate), poly(methyl methacrylate), poly(acrylic acid), poly(ethylene-co-vinyl acetate), poly(methacrylic acid), polyglycolides (PLG), polyanhydrides, poly(N-vinyl pyrrolidone), poly(vinyl alcohol), polyacrylamide, poly(ethylene glycol), polylactides (PLA), poly(lactide-co-glycolides) (PLGA), and polyorthoesters. In a preferred embodiment, the polymer used in a sustained release formulation is inert, free of leachable impurities, stable on storage, sterile, and biodegradable. In yet another embodiment, a controlled or sustained release system can be placed in proximity of the therapeutic target, *i.e.*, the lungs, thus requiring only a fraction of the systemic dose (see, *e.g.*, Goodson, in Medical Applications of Controlled Release, supra, vol. 2, pp. 115-138 (1984)).

Controlled release systems are discussed in the review by Langer (1990, Science 249:1527-1533). Any technique known to one of skill in the art can be used to produce sustained release formulations comprising one or more antibodies or antigen-binding fragments thereof. See, *e.g.*, U.S. Patent No. 4,526,938, PCT publication WO 91/05548, PCT publication WO 96/20698, Ning *et al.*, 1996, "Intratumoral Radioimmunotheraphy of a Human Colon Cancer Xenograft Using a Sustained-Release Gel," Radiotherapy & Oncology 39:179-189,.Song *et al.*, 1995, "Antibody Mediated Lung Targeting of Long-Circulating Emulsions," PDA Journal of Pharmaceutical Science & Technology 50:372-397, Cleek *et al.*, 1997, "Biodegradable Polymeric Carriers for a bFGF Antibody for Cardiovascular Application," Pro. Int'l. Symp. Control. Rel. Bioact. Mater. 24:853-854, and Lam *et al.*, 1997, "Microencapsulation of Recombinant Humanized Monoclonal Antibody for Local Delivery," Proc. Int'l. Symp. Control Rel. Bioact. Mater. 24:759-760, each of which is incorporated herein by reference in their entireties.

In certain embodiments the antibodies are administered repeatedly, wherein the administrations are separated by at least 10 days, 15 days, 30 days, 2 months, 3 months or at least 6 months. In certain embodiments the antibodies are administered repeatedly, wherein

the administrations are separated by at most 10 days, 15 days, 30 days, 2 months, 3 months or at most 6 months.

In certain embodiments, the antibodies are administered during the season of increased risk of pulmonary infections. In specific embodiments, the antibodies are administered during the RSV season.

4.4 PHARMACEUTICAL COMPOSITIONS

The present invention also provides pharmaceutical compositions. Such compositions comprise one or more of the following: (i) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof; (ii) one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof; or (iii) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant (*e.g.*, Freund's adjuvant (complete and incomplete)), excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium

carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a prophylactically or therapeutically effective amount of the antibody or fragment thereof, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a specific embodiment, the compositions of the invention may be those disclosed in U.S. Provisional Patent Application No.: 60/388,920, filed on June 14, 2002 or 60/388,921, filed on June 14, 2002, which are incorporated be reference herein in their entireties.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocamne to ease pain at the site of the injection.

Generally, the ingredients of compositions of the invention are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compositions of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the composition of the invention which will be effective in the treatment, prevention or amelioration of one or more symptoms associated with a respiratory viral infection can be determined by standard clinical techniques. For example, the dosage of the composition which will be effective in the treatment, prevention or amelioration of one or more symptoms associated with a respiratory viral infection can be determined by administering the composition to a cotton rat, measuring the RSV, PIV, and/or hMPV titer

after challenging the cotton rat with 10^5 pfu of RSV, PIV, and/or hMPV, respectively, and comparing the RSV, PIV, and/or hMPV titer, respectively, to that obtain for a cotton rat not administered the composition. Accordingly, a dosage that results in a 1 log decrease or a 90% reduction in RSV, PIV, and/or hMPV titer in the cotton rat challenged with 10^5 pfu of RSV, PIV, and/or hMPV, respectively, relative to the cotton rat challenged with 10^5 pfu of RSV, PIV, and/or hMPV, respectively, but not administered the composition is the dosage of the composition that can be administered to a human for the treatment, prevention or amelioration of symptoms associated with RSV infection. The dosage of the composition which will be effective in the treatment, prevention or amelioration of one or more symptoms associated with a respiratory, viral infection can be determined by administering the composition to an animal model (*e.g.*, a cotton rat or monkey) and measuring the serum titer of antibodies or antigen-binding fragments thereof that immunospecifically bind to a RSV, PIV, and/or hMPV antigen. Accordingly, a dosage of the composition that results in a serum titer of at least 1 μg/ml, preferably 2 μg/ml, 5 μg/ml, 10 μg/ml, 20 μg/ml, 25 μg/ml, at least 35 μg/ml, at least 40 μg/ml, at least 50 μg/ml, at least 75 μg/ml, at least 100 μg/ml, at least 125 μg/ml, at least 150 μg/ml, at least 200 μg/ml, at least 250 μg/ml, at least 300 μg/ml, at least 350 μg/ml, at least 400 μg/ml, or at least 450 μg/ml for one or all of the antibodies in the composition can be administered to a human for the treatment, prevention or amelioration of one or more symptoms associated with respiratory viral infection. In addition, *in vitro* assays may optionally be employed to help identify optimal dosage ranges.

The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the respiratory viral infection, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model (*e.g.*, the cotton rat or Cynomolgous monkey) test systems.

For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of each antibody per the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of each antibody per patient's body weight, more preferably 1 mg/kg to 10 mg/kg of each antibody per the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention or fragments thereof

may be reduced by enhancing uptake and tissue penetration (*e.g.*, into the lung) of the antibodies by modifications such as, for example, lipidation.

In a specific embodiment, antibodies of the invention or fragments thereof, or compositions comprising antibodies of the invention or fragments thereof are administered once a month, once every 6 weeks, or once every 2 months just prior to or during the RSV season. In a specific embodiment, antibodies of the invention or fragments thereof, or compositions comprising antibodies of the invention or fragments thereof are administered once a month, once every 6 weeks, or once every 2 months just prior to or during the PIV season. In a specific embodiment, antibodies of the invention or fragments thereof, or compositions comprising antibodies of the invention or fragments thereof are administered once a month, once every 6 weeks, or once every 2 months just prior to or during the hMPV season. In another embodiment, antibodies or antigen-binding fragments thereof, or compositions comprising antibodies or antigen-binding fragments thereof are administered every two months just prior to or during the RSV, PIV, or hMPV season. In yet another embodiment, antibodies or antigen-binding fragments thereof, or compositions comprising antibodies or antigen-binding fragments thereof are administered once just prior to or during the RSV, PIV, or hMPV season. The term "RSV season" refers to the season when RSV infection is most likely to occur. Typically, the RSV season in the northern hemisphere commences in November and lasts through April.

In certain embodiments, the antibodies are administered at least 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, 15 times or at least 20 times per RSV season. In certain embodiments, the antibodies are administered at most 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, 15 times or at most 20 times per RSV season. In certain embodiments, the antibodies are administered at least 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, 15 times or at least 20 times per PIV season. In certain embodiments, the antibodies are administered at most 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, 15 times or at most 20 times per PIV season. In certain embodiments, the antibodies are administered at least 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, 15 times or at least 20 times per hMPV season. In certain embodiments, the antibodies are administered at most 1 time, 2 times, 3 times, 4 times, 5 times, 6 times, 7 times, 8 times, 9 times, 10 times, 15 times or at most 20 times per hMPV season.

4.5 GENE THERAPY

In a specific embodiment, nucleic acids comprising sequences encoding antibodies that immunospecifically bind to an RSV antigen, a PIV antigen, and/or a hMPV antigen or functional derivatives thereof, are administered to treat, prevent or ameliorate one or more symptoms associated with RSV infection, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic acid. In this embodiment of the invention, the nucleic acids produce their encoded antibody or antibody fragment that mediates a prophylactic or therapeutic effect. In a specific embodiment, intrabodies are delivered to a subject via gene therapy (see section 4.1).

Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., 1993, Clinical Pharmacy 12:488-505; Wu and Wu, 1991, Biotherapy 3:87-95; Tolstoshev, 1993, Ann. Rev. Pharmacol. Toxicol. 32:573-596; Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, 1993, Ann. Rev. Biochem. 62:191-217; May, 1993, TIBTECH 11(5):155-215. Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); and Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990).

In a preferred aspect, a composition of the invention comprises nucleic acids encoding an antibody, said nucleic acids being part of an expression vector that expresses the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acids have promoters, preferably heterologous promoters, operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue- specific. In another particular embodiment, nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody encoding nucleic acids (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; Zijlstra et al., 1989, Nature 342:435-438). In specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.

Delivery of the nucleic acids into a subject may be either direct, in which case the subject is directly exposed to the nucleic acid or nucleic acid-carrying vectors, or indirect, in which case, cells are first transformed with the nucleic acids in vitro, then transplanted into the subject. These two approaches are known, respectively, as *in vivo* or *ex vivo* gene therapy.

In a specific embodiment, the nucleic acid sequences are directly administered *in vivo*, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, *e.g.*, by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, *e.g.*, by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (*e.g.*, a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, *e.g.*, Wu and Wu, 1987, J. Biol. Chem. 262:4429-4432) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted *in vivo* for cell specific uptake and expression, by targeting a specific receptor (see, *e.g.*, PCT Publications WO 92/06180; WO 92/22635; W092/203 16; W093/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, 1989, Proc. Natl. Acad. Sci. USA 86:8932-8935; and Zijlstra et al., 1989, Nature 342:435-438).

In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention or fragments thereof are used. For example, a retroviral vector can be used (see Miller et al., 1993, Meth. Enzymol. 217:581-599). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which facilitates delivery of the gene into a subject. More detail about retroviral vectors can be found in Boesen et al., 1994, Biotherapy 6:291-302, which describes the use of a retroviral vector to deliver the mdr 1 gene

to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., 1994, J. Clin. Invest. 93:644-651; Klein et al., 1994, Blood 83:1467-1473; Salmons and Gunzberg, 1993, Human Gene Therapy 4:129-141; and Grossman and Wilson, 1993, Curr. Opin. in Genetics and Devel. 3:110-114.

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, 1993, Current Opinion in Genetics and Development 3:499-503 present a review of adenovirus-based gene therapy. Bout et al., 1994, Human Gene Therapy 5:3-10 demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., 1991, Science 252:431-434; Rosenfeld et al., 1992, Cell 68:143-155; Mastrangeli et al., 1993, J. Clin. Invest. 91:225-234; PCT Publication W094/12649; and Wang et al., 1995, Gene Therapy 2:775-783. In a preferred embodiment, adenovirus vectors are used.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., 1993, Proc. Soc. Exp. Biol. Med. 204:289-300; and U.S. Patent No. 5,436,146).

Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a subject.

In this embodiment, the nucleic acid is introduced into a cell prior to administration *in vivo* of the resulting recombinant cell. Such introduction can be carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, *e.g.*, Loeffler and Behr, 1993, Meth. Enzymol. 217:599-618; Cohen et al.,

1993, Meth. Enzymol. 217:618-644; Clin. Pharma. Ther. 29:69-92 (1985)) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a subject by various methods known in the art. Recombinant blood cells (*e.g.*, hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, *e.g.*, as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the subject.

In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody or fragment thereof are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered *in vivo* for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained *in vitro* can potentially be used in accordance with this embodiment of the present invention (see *e.g.*, PCT Publication WO 94/08598; Stemple and Anderson, 1992, Cell 7 1:973-985; Rheinwald, 1980, Meth. Cell Bio. 21A:229; and Pittelkow and Scott, 1986, Mayo Clinic Proc. 61:771).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

4.6 ANTIBODY CHARACTERIZATION AND DEMONSTRATION OF THERAPEUTIC OR PROPHYLACTIC UTILITY

Antibodies may be characterized in a variety of ways. In particular, antibodies may be assayed for the ability to immunospecifically bind to a RSV antigen, a PIV antigen, and/or a hMPV antigen. Such an assay may be performed in solution (*e.g.*, Houghten, 1992, Bio/Techniques 13:412-421), on beads (Lam, 1991, Nature 354:82-84), on chips (Fodor, 1993, Nature 364:555-556), on bacteria (U.S. Patent No. 5,223,409), on spores (U.S. Patent Nos. 5,571,698; 5,403,484; and 5,223,409), on plasmids (Cull et al., 1992, Proc. Natl. Acad. Sci. USA 89:1865-1869) or on phage (Scott and Smith, 1990, Science 249:386-390; Devlin, 1990, Science 249:404-406; Cwirla et al., 1990, Proc. Natl. Acad. Sci. USA 87:6378-6382; and Felici, 1991, J. Mol. Biol. 222:301-310) (each of these references is incorporated herein in its entirety by reference). Antibodies or antigen-binding fragments thereof that have been identified to immunospecifically bind to a RSV antigen, a PIV antigen, and/or a hMPV antigen or a fragment thereof can then be assayed for their avidity and affinity for a RSV antigen, a PIV antigen, and/or a hMPV antigen.

Immunospecific binding and cross-reactivity with other antigens of an antibody may be determined by any method known in the art. Immunoassays which can be used to analyze immunospecific binding and cross-reactivity include, but are not limited to, competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays, to name but a few. Such assays are routine and well known in the art (see, *e.g.*, Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Exemplary immunoassays are described briefly below (but are not intended by way of limitation).

Immunoprecipitation protocols generally comprise lysing a population of cells in a lysis buffer such as RIPA buffer (1% NP-40 or Triton X-100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 0.01 M sodium phosphate at pH 7.2, 1% Trasylol) supplemented with protein phosphatase and/or protease inhibitors (*e.g.*, EDTA, PMSF, aprotinin, sodium vanadate), adding the antibody of interest to the cell lysate, incubating for a period of time (*e.g.*, 1 to 4 hours) at 40° C, adding protein A and/or protein G sepharose beads to the cell lysate, incubating for about an hour or more at 40° C, washing the beads in lysis buffer and resuspending the beads in SDS/sample buffer. The ability of the antibody of interest to

immunoprecipitate a particular antigen can be assessed by, *e.g.*, western blot analysis. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the binding of the antibody to an antigen and decrease the background (*e.g.*, pre-clearing the cell lysate with sepharose beads). For further discussion regarding immunoprecipitation protocols see, *e.g.*, Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.16.1.

Western blot analysis generally comprises preparing protein samples, electrophoresis of the protein samples in a polyacrylamide gel (*e.g.*, 8%- 20% SDS-PAGE depending on the molecular weight of the antigen), transferring the protein sample from the polyacrylamide gel to a membrane such as nitrocellulose, PVDF or nylon, blocking the membrane in blocking solution (*e.g.*, PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (*e.g.*, PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, *e.g.*, an anti-human antibody) conjugated to an enzymatic substrate (*e.g.*, horseradish peroxidase or alkaline phosphatase) or radioactive molecule (*e.g.*, ^{32}P or ^{125}I) diluted in blocking buffer, washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, *e.g.*, Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 10.8.1.

ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (*e.g.*, horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the

art. For further discussion regarding ELISAs see, *e.g.*, Ausubel et al, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York at 11.2.1.

The binding affinity of an antibody to an antigen and the off-rate of an antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (*e.g.*, ^{3}H or ^{125}I) with the antibody of interest in the presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of the present invention or a fragment thereof for a RSV antigen and the binding off-rates can be determined from the data by scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays. In a specific embodiment, a first antibody or an antigen-binding fragment thereof is conjugated to a labeled compound (*e.g.*, ^{3}H or ^{125}I) in the presence of increasing amounts of an unlabeled second antibody.

In a preferred embodiment, BIAcore kinetic analysis is used to determine the binding on and off rates of antibodies or antigen-binding fragments thereof to a RSV, PIV and/or hMPV antigen. BIAcore kinetic analysis comprises analyzing the binding and dissociation of a RSV antigen from chips with immobilized antibodies or antigen-binding fragments thereof on their surface (see the Example section *infra*).

The antibodies of the invention or fragments thereof can also be assayed for their ability to inhibit the binding of RSV, PIV and/or hMPV to its host cell receptor using techniques known to those of skill in the art. For example, cells expressing the receptor for RSV, PIV and/or hMPV, respectively, can be contacted with RSV, PIV and/or hMPV, respectively, in the presence or absence of an antibody or fragment thereof and the ability of the antibody or fragment thereof to inhibit RSV, PIV and/or hMPV's binding can measured by, for example, flow cytometry or a scintillation assay. RSV, PIV and/or hMPV (*e.g.*, a RSV, PIV and/or hMPV antigen such as F glycoprotein or G glycoprotein) or the antibody or antibody fragment can be labeled with a detectable compound such as a radioactive label (*e.g.*, 32P, 35S, and 125I) or a fluorescent label (*e.g.*, fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine) to enable detection of an interaction between RSV, PIV and/or hMPV and its respective host cell receptor. Alternatively, the ability of antibodies or antigen-binding fragments thereof to inhibit RSV, PIV and/or hMPV from binding to its receptor can be determined in cell-free assays. For example, RSV, PIV and/or hMPV or a RSV, PIV and/or hMPV antigen such as

G glycoprotein can be contacted with an antibody or fragment thereof and the ability of the antibody or antibody fragment to inhibit RSV, PIV and/or hMPV or the RSV, PIV and/or hMPV antigen from binding to its host cell receptor can be determined. Preferably, the antibody or the antibody fragment is immobilized on a solid support and RSV, PIV and/or hMPV, or a RSV, PIV and/or hMPV antigen is labeled with a detectable compound. Alternatively, RSV, PIV and/or hMPV, or a RSV, PIV and/or hMPV antigen is immobilized on a solid support and the antibody or fragment thereof is labeled with a detectable compound. RSV, PIV and/or hMPV, or a RSV, PIV and/or hMPV antigen may be partially or completely purified (*e.g.*, partially or completely free of other polypeptides) or part of a cell lysate. Further, a RSV, PIV and/or hMPV antigen may be a fusion protein comprising the RSV, PIV and/or hMPV antigen and a domain such as glutathionine-S-transferase. Alternatively, a RSV, PIV and/or hMPV antigen can be biotinylated using techniques well known to those of skill in the art (*e.g.*, biotinylation kit, Pierce Chemicals; Rockford, IL).

The antibodies of the invention or fragments thereof can also be assayed for their ability to inhibit or downregulate RSV, PIV and/or hMPV replication using techniques known to those of skill in the art. For example, RSV, PIV and/or hMPV replication can be assayed by a plaque assay such as described, *e.g.*, by Johnson et al., 1997, Journal of Infectious Diseases 176:1215-1224. The antibodies of the invention or fragments thereof can also be assayed for their ability to inhibit or downregulate the expression of RSV, PIV and/or hMPV polypeptides. Techniques known to those of skill in the art, including, but not limited to, Western blot analysis, Northern blot analysis, and RT-PCR can be used to measure the expression of RSV, PIV and/or hMPV polypeptides. Further, the antibodies of the invention or fragments thereof can be assayed for their ability to prevent the formation of syncytia.

The antibodies of the invention or fragments thereof are preferably tested *in vitro*, and then *in vivo* for the desired therapeutic or prophylactic activity, prior to use in humans. For example, *in vitro* assays which can be used to determine whether administration of a specific antibody or composition of the present invention is indicated, include *in vitro* cell culture assays in which a subject tissue sample is grown in culture, and exposed to or otherwise administered an antibody or composition of the present invention, and the effect of such an antibody or composition of the present invention upon the tissue sample is observed. In various specific embodiments, *in vitro* assays can be carried out with representative cells of cell types involved in a RSV, PIV and/or hMPV infection (*e.g.*, respiratory epithelial cells), to determine if an antibody or composition of the present invention has a desired effect upon

such cell types. Preferably, the antibodies or compositions comprising the antibodies are also tested in *in vitro* assays and animal model systems prior to administration to humans. In a specific embodiment, cotton rats are administered an antibody or fragment thereof, or a composition of the invention, challenged with 10^5 pfu of RSV, PIV and/or hMPV, and four or more days later the rats are sacrificed and RSV, PIV and/or hMPV titer and anti-RSV, anti-PIV and/or anti-hMPV antibody serum level is determined. Further, in accordance with this embodiment, the tissues (*e.g.*, the lung tissues) from the sacrificed rats can be examined for histological changes.

In accordance with the invention, clinical trials with human subjects need not be performed in order to demonstrate the prophylactic and/or therapeutic efficacy of antibodies of the invention or fragments thereof. *In vitro* and animal model studies using the antibodies or antigen-binding fragments thereof can be extrapolated to humans and are sufficient for demonstrating the prophylactic and/or therapeutic utility of said antibodies or antibody fragments.

Antibodies or compositions that can be used with the methods of the present invention can be tested for their toxicity in suitable animal model systems, including but not limited to rats, mice, cows, monkeys, and rabbits. For *in vivo* testing of an antibody or composition's toxicity any animal model system known in the art may be used.

The treatment is considered therapeutic if there is, for example, a reduction is viral load, amelioration of one or more symptoms, a reduction in the duration of a respiratory viral infection, or a decrease in mortality and/or morbidity following administration of an antibody or composition of the invention. Further, the treatment is considered therapeutic if there is an increase in the immune response following the administration of one or more antibodies or antigen-binding fragments thereof which immunospecifically bind to one or more RSV, PIV, and/or hMPV antigens.

Antibodies can be tested *in vitro* and *in vivo* for the ability to affect the expression levels of cytokines such as, but not limited to, IFN-α, IFN-β, IFN-γ, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12 and IL-15. In a more specific embodiment, an antibody or composition of the invention is tested for its ability to affect the expression level of one or more cytokines, the expression of which have been induced by a respiratory viral infection. In an even more specific embodiment, an antibody or composition of the invention is tested for its ability to reduce the expression level of one or more virus-induced cytokines. Techniques known to those of skill in the art can be used to measure the level of expression

of cytokines. For example, the level of expression of cytokines can be measured by analyzing the level of RNA of cytokines by, for example, RT-PCR and Northern blot analysis, and by analyzing the level of cytokines by, for example, immunoprecipitation followed by western blot analysis and ELISA. In a preferred embodiment, an antibody or composition of the invention is tested for its ability to affect the expression of IFN-γ. In a more specific embodiment, an antibody or composition of the invention is tested for its ability to affect the expression level of IFN-γ the expression of which has been induced by a respiratory viral infection. In an even more specific embodiment, an antibody or composition of the invention is tested for its ability to reduce the expression level of virus-induced IFN-γ.

Antibodies can be tested *in vitro* and *in vivo* for their ability to modulate the biological activity of immune cells, preferably human immune cells (*e.g.*, but not limited to, T-cells, B-cells, and Natural Killer cells). In more specific embodiments, antibodies can be tested *in vitro* and *in vivo* for their ability to modulate the biological activity of immune cells that has been induced by a respiratory viral infection. In even more specific embodiments, antibodies can be tested for their ability to reduce the one or more biological activities of immune cells that have been induced by a respiratory viral infection. The ability of antibodies or antigen-binding fragments thereof to modulate the biological activity of immune cells can be assessed by detecting the expression of antigens, detecting the proliferation of immune cells, detecting the activation of signaling molecules, detecting the effector function of immune cells, or detecting the differentiation of immune cells. Techniques known to those of skill in the art can be used for measuring these activities. For example, cellular proliferation can be assayed by 3H-thymidine incorporation assays and trypan blue cell counts. Antigen expression can be assayed, for example, by immunoassays including, but are not limited to, competitive and non-competitive assay systems using techniques such as western blots, immunohistochemistry radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays and FACS analysis. The activation of signaling molecules can be assayed, for example, by kinase assays and electrophoretic shift assays (EMSAs).

Antibodies can also be tested for their ability to inhibit viral replication or reduce viral load in *in vitro*, *ex vivo* and *in vivo* assays. Antibodies can also be tested for their ability to

decrease the time course of a respiratory viral infection. Antibodies can also be tested for their ability to increase the survival period of humans suffering from RSV infection by at least 25%, preferably at least 50%, at least 60%, at least 75%, at least 85%, at least 95%, or at least 99%. Further, antibodies can be tested for their ability reduce the hospitalization period of humans suffering from respiratory viral infection by at least 60%, preferably at least 75%, at least 85%, at least 95%, or at least 99%. Techniques known to those of skill in the art can be used to analyze the function of the antibodies or compositions of the invention *in vivo*.

4.7 KITS

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises (i) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof and one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof; (ii) one or more anti-PIV-antigen antibodies or antigen-binding fragments thereof and one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof; or (iii) one or more anti-RSV-antigen antibodies or antigen-binding fragments thereof, one or more anti-hMPV-antigen antibodies or antigen-binding fragments thereof. In certain embodiments, a kit comprises one or more anti-PIV-antigen antibodies, one or more anti-hMPV-antigen antibodies, and one or more anti-RSV-antigen antibodies.

In certain embodiments, the kits of the present invention further comprise a control antibody which does not react with a RSV antigen, a PIV antigen, and a hMPV antigen. In another specific embodiments, the kits of the present invention contain a means for detecting the binding of an antibody to a RSV antigen, a PIV antigen, and/or a hMPV antigen (*e.g.*, the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate). In specific embodiments, the kit may include a recombinantly produced or chemically synthesized RSV antigen, a PIV antigen, and/or a hMPV antigen. The RSV antigen, a PIV antigen, and/or a hMPV antigen provided in the kit may also be attached to a solid support.

In a more specific embodiment the detecting means of the above-described kit includes a solid support to which RSV antigen, a PIV antigen, and/or a hMPV antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the RSV antigen, a PIV antigen, and/or a hMPV antigen can be detected by binding of the said reporter-labeled antibody.

4.8. ASSAYS FOR USE WITH THE INVENTION

4.8.1 MEASUREMENT OF INCIDENCE OF INFECTION RATE

The incidence of infection can be determined by any method well-known in the art, for example, but not limited to, clinical samples (e.g., nasal swabs) can be tested for the presence of RSV, PIV, and/or hMPV by immunofluorescence assay (IFA) using an anti-RSV-antigen antibody, an anti-PIV-antigen antibody, and/or an anti-hMPV-antigen antibody, respectively. Samples containing intact cells can be directly processed, whereas isolates without intact cells should first be cultured on a permissive cell line (e.g. HEp-2 cells). Cultured cell suspensions should be cleared by centrifugation at, *e.g.*, 300xg for 5 minutes at room temperature, followed by a PBS, pH 7.4 (Ca^{++} and Mg^{++} free) wash under the same conditions. Cell pellets are resuspended in a small volume of PBS for analysis. Primary clinical isolates containing intact cells are mixed with PBS and centrifuged at 300xg for 5 minutes at room temperature. Mucus is removed from the interface with a sterile pipette tip and cell pellets are washed once more with PBS under the same conditions. Pellets are then resuspended in a small volume of PBS for analysis. Five to ten microliters of each cell suspension are spotted per 5 mm well on acetone washed 12-well HTC supercured glass slides and allowed to air dry. Slides are fixed in cold (-20oC) acetone for 10 minutes. Reactions are blocked by adding PBS - 1% BSA to each well followed by a 10 minute incubation at room temperature. Slides are washed three times in PBS - 0.1% Tween-20 and air dried. Ten microliters of each primary antibody reagent diluted to 250 ng/ml in blocking buffer is spotted per well and reactions are incubated in a humidified 37°C environment for 30 minutes. Slides are then washed extensively in three changes of PBS - 0.1% Tween-20 and air dried. Ten microliters of appropriate secondary conjugated antibody reagent diluted to 250 ng/ml in blocking buffer are spotted per respective well and reactions are incubated in a humidified 37°C environment for an additional 30 minutes. Slides are then washed in three changes of PBS - 0.1% Tween-20. Five microliters of PBS-50% glycerol-10 mM Tris pH 8.0-1 mM EDTA are spotted per reaction well, and slides are mounted with cover slips. Each

reaction well is subsequently analyzed by fluorescence microscopy at 200X power using a B-2A filter (EX 450-490 nm). Positive reactions are scored against an autofluorescent background obtained from unstained cells or cells stained with secondary reagent alone. RSV positive reactions are characterized by bright fluorescence punctuated with small inclusions in the cytoplasm of infected cells.

4.8.2 MEASUREMENT OF SERUM TITER

The antibody serum titer can be determined by any method well-known in the art, for example, but not limited to, the amount of antibody or antibody fragment in serum samples can be quantitated by a sandwich ELISA. Briefly, the ELISA consists of coating microtiter plates overnight at 4°C with an antibody that recognizes the antibody or antibody fragment in the serum. The plates are then blocked for approximately 30 minutes at room temperature with PBS-Tween-0.5% BSA. Standard curves are constructed using purified antibody or antibody fragment diluted in PBS-TWEEN-BSA, and samples are diluted in PBS-BSA-BSA. The samples and standards are added to duplicate wells of the assay plate and are incubated for approximately 1 hour at room temperature. Next, the non-bound antibody is washed away with PBS-TWEEN and the bound antibody is treated with a labeled secondary antibody (e.g., horseradish peroxidase conjugated goat-anti-human IgG) for approximately 1 hour at room temperature. Binding of the labeled antibody is detected by adding a chromogenic substrate specific for the label and measuring the rate of substrate turnover, e.g., by a spectrophotometer. The concentration of antibody or antibody fragment levels in the serum is determined by comparison of the rate of substrate turnover for the samples to the rate of substrate turnover for the standard curve.

4.8.3 BIACORE ASSAY

Determination of the kinetic parameters of antibody binding can be determined for example by the injection of 250 μL of monoclonal antibody ("mAb") at varying concentration in HBS buffer containing 0.05% Tween-20 over a sensor chip surface, onto which has been immobilized the antigen. The flow rate is maintained constant at 75uL/min. Dissociation data is collected for 15 min, or longer as necessary. Following each injection/dissociation cycle, the bound mAb is removed from the antigen surface using brief, 1 min pulses of dilute acid, typically 10-100 mM HCl, though other regenerants are employed as the circumstances warrant.

More specifically, for measurement of the rates of association, k_{on}, and dissociation, k_{off}, the antigen is directly immobilized onto the sensor chip surface through the use of standard amine coupling chemistries, namely the EDC/NHS method (EDC= N-diethylaminopropyl)-carbodiimide). Briefly, a 5-100 nM solution of the antigen in 10 mM NaOAc, pH4 or pH5 is prepared and passed over the EDC/NHS-activated surface until approximately 30-50 RU's worth of antigen are immobilized. Following this, the unreacted active esters are "capped" off with an injection of 1M Et-NH2. A blank surface, containing no antigen, is prepared under identical immobilization conditions for reference purposes. Once a suitable surface has been prepared, an appropriate dilution series of each one of the antibody reagents is prepared in HBS/Tween-20, and passed over both the antigen and reference cell surfaces, which are connected in series. The range of antibody concentrations that are prepared varies depending on what the equilibrium binding constant, K_D, is estimated to be. As described above, the bound antibody is removed after each injection/dissociation cycle using an appropriate regenerant.

Once an entire data set is collected, the resulting binding curves are globally fitted using algorithms supplied by the instrument manufacturer, BIAcore, Inc. (Piscataway, NJ). All data are fitted to a 1:1 Langmuir binding model. These algorithm calculate both the k_{on} and the k_{off}, from which the apparent equilibrium binding constant, K_D, is deduced as the ratio of the two rate constants (i.e. k_{off}/k_{on}). More detailed treatments of how the individual rate constants are derived can be found in the BIAevaluation Software Handbook (BIAcore, Inc., Piscataway, NJ).

4.8.4 MICRONEUTRALIZATION ASSAY

The ability of antibodies or antigen-binding fragments thereof to neutralize virus infectivity is determined by a microneutralization assay. This microneutralization assay is a modification of the procedures described by Anderson et al. (1985, J. Clin. Microbiol. 22:1050-1052, the disclosure of which is hereby incorporated by reference in its entirety). The procedure is also described in Johnson et al., 1999, J. Infectious Diseases 180:35-40, the disclosure of which is hereby incorporated by reference in its entirety.

Antibody dilutions are made in triplicate using a 96-well plate. Ten $TCID_{50}$ of RSV, PIV, APV, and/or hMPV are incubated with serial dilutions of the antibody or antigen-binding fragments thereof to be tested for 2 hours at 37_C in the wells of a 96-well plate. RSV susceptible cultured liver cells, such as, but not limited toHEp-2 cells (2.5×10^4) are

then added to each well and cultured for 5 days at 37_C in 5% CO_2. After 5 days, the medium is aspirated and cells are washed and fixed to the plates with 80% methanol and 20% PBS. Virus replication is then determined by viral antigen, such as F protein expression. Fixed cells are incubated with a biotin-conjugated anti-viral antigen, such as anti-F protein monoclonal antibody (*e.g.*, pan F protein, C-site-specific MAb 133-1H) washed and horseradish peroxidase conjugated avidin is added to the wells. The wells are washed again and turnover of substrate TMB (thionitrobenzoic acid) is measured at 450 nm. The neutralizing titer is expressed as the antibody concentration that causes at least 50% reduction in absorbency at 450 nm (the OD_{450}) from virus-only control cells.

4.8.5 VIRAL FUSION INHIBITION ASSAY

The ability of anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or antigen-binding fragments thereof to block RSV, PIV, and hMPV, respectively, induced fusion after viral attachment to the cells is determined in a fusion inhibition assay. This assay is identical to the microneutralization assay, except that the cells are infected with the respective virus for four hours prior to addition of antibody (Taylor et al,1992, J. Gen. Virol. 73:2217-2223).

4.8.6 ISOTHERMAL TITRATION CALORIMETRY

Thermodynamic binding affinities and enthalpies are determined from isothermal titration calorimetry (ITC) measurements on the interaction of antibodies with their respective antigen.

Antibodies are diluted in dialysate and the concentrations were determined by UV spectroscopic absorption measurements with a Perkin-Elmer Lambda 4B Spectrophotometer using an extinction coefficient of 217,000 M^{-1} cm^{-1} at the peak maximum at 280 nm. The diluted RSV-antigen, PIV-antigen, and/or hMPV-antigen concentrations are calculated from the ratio of the mass of the original sample to that of the diluted sample since its extinction coefficient is too low to determine an accurate concentration without employing and losing a large amount of sample.

<u>ITC Measurements</u>

The binding thermodynamics of the antibodies are determined from ITC measurements using a Microcal, Inc. VP Titration Calorimeter. The VP titration calorimeter consists of a matched pair of sample and reference vessels (1.409 ml) enclosed in an adiabatic

enclosure and a rotating stirrer-syringe for titrating ligand solutions into the sample vessel. The ITC measurements are performed at 25°C and 35°C. The sample vessel contained the antibody in the phosphate buffer while the reference vessel contains just the buffer solution. The phosphate buffer solution is saline 67 mM PO_4 at pH 7.4 from HyClone, Inc. Five or ten μl aliquots of the 0.05 to 0.1 mM RSV-antigen, PIV-antigen, and/or hMPV-antigen solution are titrated 3 to 4 minutes apart into the antibody sample solution until the binding is saturated as evident by the lack of a heat exchange signal.

A non-linear, least square minimization software program from Microcal, Inc., Origin 5.0, is used to fit the incremental heat of the ith titration (ΔQ (i)) of the total heat, Q_t, to the total titrant concentration, X_t, according to the following equations (I),

$$Q_t = nC_t\Delta H_b{}^{\circ}V\{1 + X_t/nC_t + 1/nK_bC_t - [(1 + X_t/nC_t + 1/nK_bC_t)^2 - 4X_t/nC_t]^{1/2}\}/2 \quad (1\text{ a})$$

$$\Delta Q(i) = Q(i) + dVi/2V\ \{Q(i) + Q(i\text{-}1)\} - Q(i\text{-}1) \quad (1b)$$

where C_t is the initial antibody concentration in the sample vessel, V is the volume of the sample vessel, and n is the stoichiometry of the binding reaction, to yield values of K_b, $\Delta H_b{}^{\circ}$, and n. The optimum range of sample concentrations for the determination of K_b depends on the value of K_b and is defined by the following relationship.

$$C_t\ K_b\ n \leq 500 \quad (2)$$

so that at 1 μM the maximum K_b that can be determined is less than 2.5 X 10^8 M^{-1}. If the first titrant addition does not fit the binding isotherm, it was neglected in the final analysis since it may reflect release of an air bubble at the syringe opening-solution interface.

4.8.7 COTTON RAT PROPHYLAXIS

This assay is used to determine the ability of anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies or fragments thereof to prevent lower respiratory tract viral infection in cotton rats when administered by intravenous (IV) route. In certain other embodiments, the antibodies are administered by intramuscular (IM) route or by intranasal route (IN). The antibodies can be administered by any technique well-known to the skilled artisan. This assay is also used to correlate the serum concentration of anti-RSV-antigen antibodies, anti-PIV-antigen antibodies, and/or anti-hMPV-antigen antibodies with a reduction in lung RSV, PIV, and/or hMPV, respectively, titer.

Bovine serum albumin (BSA; fraction V) can be obtained from Sigma Chemicals. RSV-Long (A subtype), RSV B subtype, PIV, or hMPV is propagated in cultured liver cells, such as, but not limited to Hep-2 cells. On day 0, groups of cotton rats (*Sigmodon*

hispidis, average weight 100 g) are administered the antibody of interest or BSA by intramuscular injection, by intravenous injection, or by intranasal route. Four days after the infection, animals are sacrificed, and their lung tissue is harvested and pulmonary virus titers are determined by plaque titration. In certain embodiments, 0.31, 0.63, 1.25, 2.5, 5.5 and 10 mg/kg (body weight) of antibody are administered. Bovine serum albumin (BSA) 10 mg/kg is used as a negative control. Antibody concentrations in the serum at the time of challenge are determined using a sandwich ELISA.

4.8.8 BIOAVAILABILITY

The percent of dose entering the systemic circulation after administration of a given dosage of antibodies (drug) is referred to as bioavailability. More explicitly, bioavailability is defined as the ratio of the amount of antibodies "absorbed" from a test formulation to the amount "absorbed" after administration of a standard formulation. Frequently, the "standard formulation" used in assessing bioavailability is the aqueous solution of the drug, given intravenously.

The amount of antibodies absorbed is taken as a measure of the ability of the formulation to deliver the antibodies to the sites of drug action; this will depend on such factors as, *e.g.*, disintegration and dissolution properties of the dosage form, and the rate of biotransformation relative to rate of absorption - dosage forms containing identical amounts of active drug may differ markedly in their abilities to make drug available, and therefore, in their abilities to permit the drug to manifest its expected pharmacodynamic and therapeutic properties.

"Amount absorbed" is conventionally measured by one of two criteria, either the area under the *time-plasma concentration curve (AUC)* or the *total (cumulative) amount of drug excreted* in the urine following drug administration. A linear relationship exists between "area under the curve" and dose when the fraction of drug absorbed is independent of dose, and elimination rate (half-life) and volume of distribution are independent of dose and dosage form. A linearity of the relationship between area under the curve and dose may occur if, for example, the absorption process is a saturable one, or if drug fails to reach the systemic circulation because of, e.g., binding of drug in the intestine or biotransformation in the liver during the drug's first transit through the portal system.

4.8.9 CLINICAL TRIALS

Antibodies of the invention or fragments thereof tested in *in vitro* assays and animal models may be further evaluated for safety, tolerance and pharmacokinetics in groups of normal healthy adult volunteers. The volunteers are administered intramuscularly, intravenously or by a pulmonary delivery system a single dose of 0.5 mg/kg, 3 mg/kg, 5 mg/kg, 10 mg/kg or 15 mg/kg of an antibody or fragment thereof which immunospecifically binds to a RSV, PIV, and/or hMPV antigen. Each volunteer is monitored at least 24 hours prior to receiving the single dose of the antibody or fragment thereof and each volunteer will be monitored for at least 48 hours after receiving the dose at a clinical site. Then volunteers are monitored as outpatients on days 3, 7, 14, 21, 28, 35, 42, 49, and 56 postdose.

Blood samples are collected via an indwelling catheter or direct venipuncture using 10 ml red-top Vacutainer tubes at the following intervals: (1) prior to administering the dose of the antibody or antibody fragment; (2) during the administration of the dose of the antibody or antibody fragment; (3) 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 24 hours, and 48 hours after administering the dose of the antibody or antibody fragment; and (4) 3 days, 7 days 14 days, 21 days, 28 days, 35 days, 42 days, 49 days, and 56 days after administering the dose of the antibody or antibody fragment. Samples are allowed to clot at room temperature and serum will be collected after centrifugation.

The antibody or antibody fragment is partially purified from the serum samples and the amount of antibody or antibody fragment in the samples will be quantitated by ELISA. Briefly, the ELISA consists of coating microtiter plates overnight at 4°C with an antibody that recognizes the antibody or antibody fragment administered to the volunteer. The plates are then blocked for approximately 30 minutes at room temperate with PBS-Tween-0.5% BSA. Standard curves are constructed using purified antibody or antibody fragment, not administered to a volunteer. Samples are diluted in PBS-Tween-BSA. The samples and standards are incubated for approximately 1 hour at room temperature. Next, the bound antibody is treated with a labeled antibody (*e.g.*, horseradish peroxidase conjugated goat-anti-human IgG) for approximately 1 hour at room temperature. Binding of the labeled antibody is detected, *e.g.*, by a spectrophotometer.

The concentration of antibody or antibody fragment levels in the serum of volunteers are corrected by subtracting the predose serum level (background level) from the serum levels at each collection interval after administration of the dose. For each volunteer the pharmacokinetic parameters are computed according to the model-independent approach

(Gibaldi et al., eds., 1982, *Pharmacokinetics*, 2nd edition, Marcel Dekker, New York) from the corrected serum antibody or antibody fragment concentrations.

4.8.10 METHODS TO IDENTIFY MPV

The invention encompasses treatment of any isolates of MPV, including those which are characterized as belonging to the subgroups and variants described in section 4.1.7.1, or belonging to a yet to be characterized subgroup or variant.

Immunoassays can be used in order to characterize the protein components that are present in a given sample. Immunoassays are an effective way to compare viral isolates using peptides components of the viruses for identification. For example, a method for identifying an isolates of MPV comprises inoculating an essentially MPV-uninfected or specific-pathogen-free guinea pig or ferret (in the detailed description the animal is inoculated intranasally but other was of inoculation such as intramuscular or intradermal inoculation, and using an other experimental animal, is also feasible) with the prototype isolate I-2614 or related isolates. Sera are collected from the animal at day zero, two weeks and three weeks post inoculation. The animal specifically seroconverted as measured in virus neutralization (VN) assay and indirect immunofluorescence assay against the respective isolate I-2614 and the sera from the seroconverted animal are used in the immunological detection of said further isolates. As an example, the invention provides the characterization of a new member in the family of *Paramyxoviridae*, a human metapneumovirus or metapneumovirus-like virus (since its final taxonomy awaits discussion by a viral taxonomy committee the MPV is herein for example described as taxonomically corresponding to APV) (MPV) which may cause severe respiratory tract infection in humans. The clinical signs of the disease caused by MPV are essentially similar to those caused by hRSV, such as cough, myalgia, vomiting, fever broncheolitis or pneumonia, possible conjunctivitis, or combinations thereof. As is seen with hRSV infected children, specifically very young children may require hospitalization. As an example an MPV which was deposited January 19, 2001 as I-2614 with CNCM, Institute Pasteur, Paris or a virus isolate phylogenetically corresponding therewith can be used

4.8.10.1 PHYLOGENETIC ANALYSIS

Phylogenetic relationships between isolates of mammalian MPV can be evaluated by the methods set forth below or any other technique known to the skilled artisan. Many

methods or approaches are available to analyze phylogenetic relationship; these include distance, maximum likelihood, and maximum parsimony methods (Swofford, DL., et. al., Phylogenetic Inference. In Molecular Systematics. Eds. Hillis, DM, Mortiz, C, and Mable, BK. 1996. Sinauer Associates: Massachusetts, USA. pp. 407 - 514; Felsenstein, J., 1981, J. Mol. Evol. 17:368-376). In addition, bootstrapping techniques are an effective means of preparing and examining confidence intervals of resultant phylogenetic trees (Felsenstein, J., 1985, Evolution. 29:783-791). Any method or approach using nucleotide or peptide sequence information to compare mammalian MPV isolates can be used to establish phylogenetic relationships, including, but not limited to, distance, maximum likelihood, and maximum parsimony methods or approaches. Any method known in the art can be used to analyze the quality of phylogenetic data, including but not limited to bootstrapping. Alignment of nucleotide or peptide sequence data for use in phylogenetic approaches, include but are not limited to, manual alignment, computer pairwise alignment, and computer multiple alignment. One skilled in the art would be familiar with the preferable alignment method or phylogenetic approach to be used based upon the information required and the time allowed.

In one embodiment, a DNA maximum likehood method is used to infer relationships between hMPV isolates. In another embodiment, bootstrapping techniques are used to determine the certainty of phylogenetic data created using one of said phylogenetic approaches. In another embodiment, jumbling techniques are applied to the phylogenetic approach before the input of data in order to minimize the effect of sequence order entry on the phylogenetic analyses. In one specific embodiment, a DNA maximum likelihood method is used with bootstrapping. In another specific embodiment, a DNA maximum likelihood method is used with bootstrapping and jumbling. In another more specific embodiment, a DNA maximum likelihood method is used with 50 bootstraps. In another specific embodiment, a DNA maximum likelihood method is used with 50 bootstraps and 3 jumbles. In another specific embodiment, a DNA maximum likelihood method is used with 100 bootstraps and 3 jumbles.

In one embodiment, nucleic acid or peptide sequence information from an isolate of hMPV is compared or aligned with sequences of other hMPV isolates. The amino acid sequence can be the amino acid sequence of the L protein, the M protein, the N protein, the P protein, or the F protein. In another embodiment, nucleic acid or peptide sequence information from an hMPV isolate or a number of hMPV isolates is compared or aligned

with sequences of other viruses. In another embodiment, phylogenetic approaches are applied to sequence alignment data so that phylogenetic relationships can be inferred and/or phylogenetic trees constructed. Any method or approach that uses nucleotide or peptide sequence information to compare hMPV isolates can be used to infer said phylogenetic relationships, including, but not limited to, distance, maximum likelihood, and maximum parsimony methods or approaches.

Other methods for the phylogenetic analysis are disclosed in International Patent Application PCT/NL02/00040, published as WO 02/057302, which is incorporated in its entirety herein. In particular, PCT/NL02/00040 discloses nucleic acid sequences that are suitable for phylogenetic analysis at page 12, line 27 to page 19, line29, which is incorporated herein by reference.

For the phylogenetic analyses it is most useful to obtain the nucleic acid sequence of a non-MPV as outgroup with which the virus is to be compared, a very useful outgroup isolate can be obtained from avian pneumovirus serotype C (APV-C), see, *e.g.*, Figure 16.

Many methods and programs are known in the art and can be used in the inference of phylogenetic relationships, including, but not limited to BioEdit, ClustalW, TreeView, and NJPlot. Methods that would be used to align sequences and to generate phylogenetic trees or relationships would require the input of sequence information to be compared. Many methods or formats are known in the art and can be used to input sequence information, including, but not limited to, FASTA, NBRF, EMBL/SWISS, GDE protein, GDE nucleotide, CLUSTAL, and GCG/MSF. Methods that would be used to align sequences and to generate phylogenetic trees or relationships would require the output of results. Many methods or formats can be used in the output of information or results, including, but not limited to, CLUSTAL, NBRF/PIR, MSF, PHYLIP, and GDE. In one embodiment, ClustalW is used in conjunction with DNA maximum likelihood methods with 100 bootstraps and 3 jumbles in order to generate phylogenetic relationships.

4.8.10.2 ALIGNMENT OF SEQUENCES

Two or more amino acid sequences can be compared by BLAST (Altschul, S.F. *et al.*, 1990, J. Mol. Biol. 215:403-410) to determine their sequence homology and sequence identities to each other. Two or more nucleotide sequences can be compared by BLAST (Altschul, S.F. *et al.*, 1990, J. Mol. Biol. 215:403-410) to determine their sequence homology and sequence identities to each other. BLAST comparisons can be performed using the

Clustal W method (MacVector™). In certain specific embodiments, the alignment of two or more sequences by a computer program can be followed by manual re-adjustment.

The determination of percent identity between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2264-2268, modified as in Karlin and Altschul, 1993, Proc. Natl. Acad. Sci. USA 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul et al., 1990, J. Mol. Biol. 215:403-410. BLAST nucleotide comparisons can be performed with the NBLAST program. BLAST amino acid sequence comparisons can be performed with the XBLAST program. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, 1997, Nucleic Acids Res.25:3389-3402. Alternatively, PSI-Blast can be used to perform an iterated search which detects distant relationships between molecules (Altschul *et al.*, 1997, *supra*). When utilizing BLAST, Gapped BLAST, and PSI-Blast programs, the default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used (*see*http://www.ncbi.nlm.nih.gov). Another preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, 1988, CABIOS 4:11-17. Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table can be used. The gap length penalty can be set by the skilled artisan. The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, typically only exact matches are counted.

4.8.10.3 HYBRIDIZATION CONDITIONS

A nucleic acid which is hybridizable to a nucleic acid of a mammalian MPV, or to its reverse complement, or to its complement can be used in the methods of the invention to determine their sequence homology and identities to each other. In certain embodiments, the nucleic acids are hybridized under conditions of high stringency. By way of example and not limitation, procedures using such conditions of high stringency are as follows. Prehybridization of filters containing DNA is carried out for 8 h to overnight at 65 C in buffer composed of 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll,

0.02% BSA, and 500 μg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65 C in prehybridization mixture containing 100 μg/ml denatured salmon sperm DNA and 5-20 X 106 cpm of 32P-labeled probe. Washing of filters is done at 37 C for 1 h in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1X SSC at 50 C for 45 min before autoradiography. Other conditions of high stringency which may be used are well known in the art. In other embodiments of the invention, hybridization is performed under moderate of low stringency conditions, such conditions are well-known to the skilled artisan (*see* e.g., Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York; see also, Ausubel et al., eds., in the Current Protocols in Molecular Biology series of laboratory technique manuals, 1987-1997 Current Protocols,© 1994-1997 John Wiley and Sons, Inc.).

TABLE 5: LEGEND FOR SEQUENCE LISTING

SEQ ID NO:1	Human metapneumovirus isolate 00-1 matrix protein (M) and fusion protein (F) genes
SEQ ID NO:2	Avian pneumovirus fusion protein gene, partial cds
SEQ ID NO:3	Avian pneumovirus isolate 1b fusion protein mRNA,complete cds
SEQ ID NO:4	Turkey rhinotracheitis virus gene for fusion protein (F1 and F2 subunits), complete cds
SEQ ID NO:5	Avian pneumovirus matrix protein (M) gene, partial cds and Avian pneumovirus fusion glycoprotein (F) gene, complete cds
SEQ ID NO:6	paramyxovirus F protein hRSV B
SEQ ID NO:7	paramyxovirus F protein hRSV A2
SEQ ID NO:8	human metapneumovirus01-71 (partial sequence)
SEQ ID NO:9	Human metapneumovirus isolate 00-1 matrix protein(M) and fusion protein (F) genes
SEQ ID NO:10	Avian pneumovirus fusion protein gene, partial cds
SEQ ID NO:11	Avian pneumovirus isolate 1b fusion protein mRNA,complete cds
SEQ ID NO:12	Turkey rhinotracheitis virus gene for fusion protein (F1 and F2 subunits), complete cds
SEQ ID NO:13	Avian pneumovirus fusion glycoprotein (F) gene, complete cds
SEQ ID NO:14	Turkey rhinotracheitis virus (strain CVL14/1)attachment protien (G) mRNA, complete cds
SEQ ID NO:15	Turkey rhinotracheitis virus (strain 6574)attachment protein (G), complete cds
SEQ ID NO:16	Turkey rhinotracheitis virus (strain CVL14/1)attachment protein (G) mRNA, complete cds

SEQ ID NO:17 Turkey rhinotracheitis virus (strain 6574)attachment protein (G), complete cds
SEQ ID NO:18 isolate NL/1/99 (99-1) HMPV (Human Metapneumovirus)cDNA sequence
SEQ ID NO:19 isolate NL/1/00 (00-1) HMPV cDNA sequence
SEQ ID NO:20 isolate NL/17/00 HMPV cDNA sequence
SEQ ID NO:21 isolate NL/1/94 HMPV cDNA sequence
SEQ ID NO:22 RT-PCR primer TR1
SEQ ID NO:23 RT-PCR primer N1
SEQ ID NO:24 RT-PCR primer N2
SEQ ID NO:25 RT-PCR primer M1
SEQ ID NO:26 RT-PCR primer M2
SEQ ID NO:27 RT-PCR primer F1
SEQ ID NO:28 RT-PCR primer N3
SEQ ID NO:29 RT-PCR primer N4
SEQ ID NO:30 RT-PCR primer M3
SEQ ID NO:31 RT-PCR primer M4
SEQ ID NO:32 RT-PCR primer F7
SEQ ID NO:33 RT-PCR primer F8
SEQ ID NO:34 RT-PCR primer L6
SEQ ID NO:35 RT-PCR primer L7
SEQ ID NO:36 Oligonucleotide probe M
SEQ ID NO:37 Oligonucleotide probe N
SEQ ID NO:38 Oligonucleotide probe L
SEQ ID NO:39 TaqMan primer and probe sequences for isolates NL/1/00, BI/1/01, FI/4/01, NL/8/01, FI/2/01
SEQ ID NO:40 TaqMan primer and probe sequences for isolates NL/30/01
SEQ ID NO:41 TaqMan primer and probe sequences for isolates NL/22/01 and NL/23/01
SEQ ID NO:42 TaqMan primer and probe sequences for isolate NL/17/01
SEQ ID NO:43 TaqMan primer and probe sequences for isolate NL/17/00
SEQ ID NO:44 TaqMan primer and probe sequences for isolates NL/9/01, NL/21/01, and NL/5/01
SEQ ID NO:45 TaqMan primer and probe sequences for isolates FI/1/01 and FI/10/01
SEQ ID NO:46 Primer ZF1
SEQ ID NO:47 Primer ZF4
SEQ ID NO:48 Primer ZF7
SEQ ID NO:49 Primer ZF10
SEQ ID NO:50 Primer ZF13
SEQ ID NO:51 Primer ZF16
SEQ ID NO:52 Primer CS1
SEQ ID NO:53 Primer CS4
SEQ ID NO:54 Primer CS7
SEQ ID NO:55 Primer CS10
SEQ ID NO:56 Primer CS13
SEQ ID NO:57 Primer CS16

SEQ ID NO:58 Forward primer for amplification of HPIV-1
SEQ ID NO:59 Reverse primer for amplification of HPIV-1
SEQ ID NO:60 Forward primer for amplification of HPIV-2
SEQ ID NO:61 Reverse primer for amplification of HPIV-2
SEQ ID NO:62 Forward primer for amplification of HPIV-3
SEQ ID NO:63 Reverse primer for amplification of HPIV-3
SEQ ID NO:64 Forward primer for amplification of HPIV-4
SEQ ID NO:65 Reverse primer for amplification of HPIV-4
SEQ ID NO:66 Forward primer for amplification of Mumps
SEQ ID NO:67 Reverse primer for amplification of Mumps
SEQ ID NO:68 Forward primer for amplification of NDV
SEQ ID NO:69 Reverse primer for amplification of NDV
SEQ ID NO:70 Forward primer for amplification of Tupaia
SEQ ID NO:71 Reverse primer for amplification of Tupaia
SEQ ID NO:72 Forward primer for amplification of Mapuera
SEQ ID NO:73 Reverse primer for amplification of Mapuera
SEQ ID NO:74 Forward primer for amplification of Hendra
SEQ ID NO:75 Reverse primer for amplification of Hendra
SEQ ID NO:76 Forward primer for amplification of Nipah
SEQ ID NO:77 Reverse primer for amplification of Nipah
SEQ ID NO:78 Forward primer for amplification of HRSV
SEQ ID NO:79 Reverse primer for amplification of HRSV
SEQ ID NO:80 Forward primer for amplification of Measles
SEQ ID NO:81 Reverse primer for amplification of Measles
SEQ ID NO:82 Forward primer to amplify general paramyxoviridae viruses
SEQ ID NO:83 Reverse primer to amplify general paramyxoviridae viruses
SEQ ID NO:84 G-gene coding sequence for isolate NL/1/00 (A1)
SEQ ID NO:85 G-gene coding sequence for isolate BR/2/01 (A1)
SEQ ID NO:86 G-gene coding sequence for isolate FL/4/01 (A1)
SEQ ID NO:87 G-gene coding sequence for isolate FL/3/01 (A1)
SEQ ID NO:88 G-gene coding sequence for isolate FL/8/01 (A1)
SEQ ID NO:89 G-gene coding sequence for isolate FL/10/01 (A1)
SEQ ID NO:90 G-gene coding sequence for isolate NL/10/01 (A1)
SEQ ID NO:91 G-gene coding sequence for isolate NL/2/02 (A1)
SEQ ID NO:92 G-gene coding sequence for isolate NL/17/00 (A2)
SEQ ID NO:93 G-gene coding sequence for isolate NL/1/81 (A2)
SEQ ID NO:94 G-gene coding sequence for isolate NL/1/93 (A2)
SEQ ID NO:95 G-gene coding sequence for isolate NL/2/93 (A2)
SEQ ID NO:96 G-gene coding sequence for isolate NL/3/93 (A2)
SEQ ID NO:97 G-gene coding sequence for isolate NL/1/95 (A2)
SEQ ID NO:98 G-gene coding sequence for isolate NL/2/96 (A2)
SEQ ID NO:99 G-gene coding sequence for isolate NL/3/96 (A2)
SEQ ID NO:100 G-gene coding sequence for isolate NL/22/01 (A2)
SEQ ID NO:101 G-gene coding sequence for isolate NL/24/01 (A2)
SEQ ID NO:102 G-gene coding sequence for isolate NL/23/01 (A2)

SEQ ID NO:103 G-gene coding sequence for isolate NL/29/01 (A2)
SEQ ID NO:104 G-gene coding sequence for isolate NL/3/02 (A2)
SEQ ID NO:105 G-gene coding sequence for isolate NL/1/99 (B1)
SEQ ID NO:106 G-gene coding sequence for isolate NL/11/00 (B1)
SEQ ID NO:107 G-gene coding sequence for isolate NL/12/00 (B1)
SEQ ID NO:108 G-gene coding sequence for isolate NL/5/01 (B1)
SEQ ID NO:109 G-gene coding sequence for isolate NL/9/01 (B1)
SEQ ID NO:110 G-gene coding sequence for isolate NL/21/01 (B1)
SEQ ID NO:111 G-gene coding sequence for isolate NL/1/94 (B2)
SEQ ID NO:112 G-gene coding sequence for isolate NL/1/82 (B2)
SEQ ID NO:113 G-gene coding sequence for isolate NL/1/96 (B2)
SEQ ID NO:114 G-gene coding sequence for isolate NL/6/97 (B2)
SEQ ID NO:115 G-gene coding sequence for isolate NL/9/00 (B2)
SEQ ID NO:116 G-gene coding sequence for isolate NL/3/01 (B2)
SEQ ID NO:117 G-gene coding sequence for isolate NL/4/01 (B2)
SEQ ID NO:118 G-gene coding sequence for isolate UK/5/01 (B2)
SEQ ID NO:119 G-protein sequence for isolate NL/1/00 (A1)
SEQ ID NO:120 G-protein sequence for isolate BR/2/01 (A1)
SEQ ID NO:121 G-protein sequence for isolate FL/4/01 (A1)
SEQ ID NO:122 G-protein sequence for isolate FL/3/01 (A1)
SEQ ID NO:123 G-protein sequence for isolate FL/8/01 (A1)
SEQ ID NO:124 G-protein sequence for isolate FL/10/01 (A1)
SEQ ID NO:125 G-protein sequence for isolate NL/10/01 (A1)
SEQ ID NO:126 G-protein sequence for isolate NL/2/02 (A1)
SEQ ID NO:127 G-protein sequence for isolate NL/17/00 (A2)
SEQ ID NO:128 G-protein sequence for isolate NL/1/81 (A2)
SEQ ID NO:129 G-protein sequence for isolate NL/1/93 (A2)
SEQ ID NO:130 G-protein sequence for isolate NL/2/93 (A2)
SEQ ID NO:131 G-protein sequence for isolate NL/3/93 (A2)
SEQ ID NO:132 G-protein sequence for isolate NL/1/95 (A2)
SEQ ID NO:133 G-protein sequence for isolate NL/2/96 (A2)
SEQ ID NO:134 G-protein sequence for isolate NL/3/96 (A2)
SEQ ID NO:135 G-protein sequence for isolate NL/22/01 (A2)
SEQ ID NO:136 G-protein sequence for isolate NL/24/01 (A2)
SEQ ID NO:137 G-protein sequence for isolate NL/23/01 (A2)
SEQ ID NO:138 G-protein sequence for isolate NL/29/01 (A2)
SEQ ID NO:139 G-protein sequence for isolate NL/3/02 (A2)
SEQ ID NO:140 G-protein sequence for isolate NL/1/99 (B1)
SEQ ID NO:141 G-protein sequence for isolate NL/11/00 (B1)
SEQ ID NO:142 G-protein sequence for isolate NL/12/00 (B1)
SEQ ID NO:143 G-protein sequence for isolate NL/5/01 (B1)
SEQ ID NO:144 G-protein sequence for isolate NL/9/01 (B1)
SEQ ID NO:145 G-protein sequence for isolate NL/21/01 (B1)
SEQ ID NO:146 G-protein sequence for isolate NL/1/94 (B2)
SEQ ID NO:147 G-protein sequence for isolate NL/1/82 (B2)
SEQ ID NO:148 G-protein sequence for isolate NL/1/96 (B2)

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SEQ ID NO:163 F-gene coding sequence for isolate UK/7/01
SEQ ID NO:164 F-gene coding sequence for isolate FL/10/01
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SEQ ID NO:166 F-gene coding sequence for isolate NL/8/01
SEQ ID NO:167 F-gene coding sequence for isolate NL/10/01
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SEQ ID NO:214 F-gene coding sequence for isolate FL/9/01
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SEQ ID NO:224 F-gene coding sequence for isolate NL/3/01
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SEQ ID NO:241 F-protein sequence for isolate FL/8/01
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SEQ ID NO:390 attachment glycoprotein of Human respiratory syncytial virus
SEQ ID NO:391 fusion glycoprotein of Human respiratory syncytial virus
SEQ ID NO:392 small hydrophobic protein of Human respiratory syncytial virus
SEQ ID NO:393 RNA polymerase beta subunit (Large structural protein) (L protein) of Human respiratory syncytial virus
SEQ ID NO:394 phosphoprotein P of Human respiratory syncytial virus
SEQ ID NO:395 attachment glycoprotein G of Human respiratory syncytial virus
SEQ ID NO:396 nucleocapsid protein of Human respiratory syncytial virus
SEQ ID NO:397 nucleoprotein (N) of Human respiratory syncytial virus
SEQ ID NO:398 matrix protein of Human respiratory syncytial virus
SEQ ID NO:399 Nucleoprotein (N)
SEQ ID NO:400 Phosphoprotein (P)
SEQ ID NO:401 Matrix Protein (M)
SEQ ID NO:402 Matrix Protein 2-1 (M2)
SEQ ID NO:403 Matrix Protein 2-2 (M2)
SEQ ID NO:404 Small Hydrophobic Protein (SH)
SEQ ID NO:405 RNA-dependent RNA polymerase (L) of Human metapneumovirus
SEQ ID NO:406 RNA-dependent RNA polymerase (L) of Human metapneumovirus
SEQ ID NO:407 RNA polymerase alpha subunit (Nucleocapsid phosphoprotein) of Human parainfluenza 1 virus
SEQ ID NO:408 L polymerase protein of Human parainfluenza 1 virus
SEQ ID NO:409 HN glycoprotein of Human parainfluenza 1 virus
SEQ ID NO:410 matrix protein of Human parainfluenza 1 virus
SEQ ID NO:411 Y1 protein of Human parainfluenza 1 virus
SEQ ID NO:412 C protein of Human parainfluenza 1 virus
SEQ ID NO:413 phosphoprotein of Human parainfluenza 1 virus
SEQ ID NO:414 nucleoprotein of Human parainfluenza 1 virus
SEQ ID NO:415 F glycoprotein of Human parainfluenza 1 virus
SEQ ID NO:416 D protein of Human parainfluenza virus 3
SEQ ID NO:417 hemagglutinin-neuraminidase of Human parainfluenza virus 3
SEQ ID NO:418 nucleocapsid protein of Human parainfluenza virus 3
SEQ ID NO:419 P protein of Human parainfluenza virus 2
SEQ ID NO:420 F protein of Human parainfluenza virus
SEQ ID NO:421 G protein of Human parainfluenza virus
SEQ ID NO:422 Homo sapiens

SEQ ID NO:423 Homo sapiens
SEQ ID NO:424 Avian pneumovirus fusion protein gene
SEQ ID NO:425 Avian pneumovirus isolate 1b fusion protein mRNA
SEQ ID NO:426 Turkey rhinotracheitis virus gene for fusion protein (F1 and F2 subunits), complete cds
SEQ ID NO:427 Avian pneumovirus fusion glycoprotein (F) gene, complete cds
SEQ ID NO:428 Turkey rhinotracheitis virus (strain CVL14/1) attachment protien (G) mRNA, complete cds
SEQ ID NO:429 Turkey rhinotracheitis virus (strain 6574) attachment protein (G)
SEQ ID NO:430 Postulated HRA sequence of strain NL1/00
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SEQ ID NO:436 Postulated HRB sequence of strain NL1/99
SEQ ID NO:437 Postulated HRB sequence of strain NL1/94

Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

All publications, patents and patent applications mentioned in this specification are herein incorporated by reference into the specification to the same extent as if each individual publication, patent or patent application was specifically and individually indicated to be incorporated herein by reference.

WHAT IS CLAIMED IS:

1. A method of preventing a viral infection in a subject, said method comprising administering to the subject:

(i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen.

2. The method of claim 1, wherein one or more of said first antibodies or antigen-binding fragments thereof neutralize RSV.

3. The method of claim 1, wherein one or more of said second antibodies or antigen-binding fragments thereof neutralize hMPV.

4. The method of claim 1, wherein one or more of said first antibodies or antigen-binding fragments thereof block RSV infection of cells of the subject.

5. The method of claim 1, wherein one or more of said second antibodies or antigen-binding fragments thereof block hMPV infection of cells of the subject.

6. A method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject:

(i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen.

7. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or a fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or a fragments thereof bind immunospecifically to a hMPV antigen,

wherein the first dose reduces the incidence of RSV infection by at least 25% and wherein the second dose reduces the incidence of hMPV infection by at least 25%.

8. The method of claim 7, wherein the first dose reduces the incidence of RSV infection by at least 50% and wherein the second dose reduces the incidence of hMPV infection by at least 50%.

9. The method of claim 7, wherein the first dose reduces the incidence of RSV infection by at least 75% and wherein the second dose reduces the incidence of hMPV infection by at least 75%.

10. The method of claim 7, wherein the first dose reduces the incidence of RSV infection by at least 90% and wherein the second dose reduces the incidence of hMPV infection by at least 90%.

11. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen,

wherein the serum titer of one or more of said first antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said first antibodies or antigen-binding fragments thereof and wherein the serum titer of one or more of said second antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said second antibodies or antigen-binding fragments thereof.

12. The method of claim 1, 6, 7, or 11, wherein the amino acid sequence of the RSV antigen is that of SEQ ID NO:390 to 398, respectively.

13. The method of claim 1, 6, 7, or 11, wherein the amino acid sequence of the RSV antigen is 90% identical to the amino acid sequence of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, or RSV G protein.

14. The method of claim 1, 6, 7, or 11, wherein the RSV antigen is selected from the group consisting of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, and RSV G protein.

15. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies immunospecifically bind to an antigen of Group A or Group B RSV.

16. The method of claim 1, 6, 7, or 11, wherein the RSV antigen is RSV F protein.

17. The method of claim 1, 6, 7, or 11, wherein one or more of said second antibodies cross-react with a turkey APV antigen.

18. The method of claim 1, 6, 7, or 11, wherein one or more of said second antibodies are (i) human or humanized antibodies and (ii) cross-react with a turkey APV antigen.

19. The method of claim 17, wherein said turkey APV antigen is selected from the group consisting of turkey APV nucleoprotein, turkey APV phosphoprotein, turkey APV matrix protein, turkey APV small hydrophobic protein, turkey APV RNA-dependent RNA polymerase, turkey APV F protein, and turkey APV G protein.

20. The method of claim 17, wherein said turkey APV antigen is an antigen of avian pneumovirus type A, avian pneumovirus type B, or avian pneumovirus type C.

21. The method of claim 17, wherein the amino acid sequence of said turkey APV antigen is that of SEQ ID NO:424 to 429, respectively.

22. The method of claim 1, 6, 7, or 11, wherein the amino acid sequence of the hMPV antigen is that of SEQ ID NO: 399-406, 420, or 421, respectively.

23. The method of claim 1, 6, 7, or 11, wherein the hMPV antigen is selected from the group consisting of hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and hMPV G protein.

24. The method of claim 1, 6, 7, or 11, wherein the hMPV antigen is hMPV F protein.

25. The method of claim 1, 6, 7, or 11, wherein the first antibody is Palivizumab; AFFF; P12f2 P12f4; P11d4; Ale9; A12a6; A13c4; A17d4; A4B4; 1X-493L1; FR H3-3F4; M3H9; Y10H6; DG; AFFF(1); 6H8; L1-7E5; L2-15B10; A13a11; A1h5; A4B4(1);A4B4-F52S; or A4B4L1FR-S28R.

26. The method of claim 1 or 6, wherein the effective amount of one or more of said first antibodies is 15 mg/kg or less.

27. The method of claim 1 or 6, wherein the effective amount of one or more of said first antibodies is 10 mg/kg or less.

28. The method of claim 1 or 6, wherein the effective amount of one or more of said first antibodies is 1 mg/kg or less.

29. The method of claim 1 or 6, wherein the effective amount of one or more of said second antibodies or antigen-binding fragments thereof is 15 mg/kg or less.

30. The method of claim 1 or 6, wherein the effective amount of one or more of said second antibodies or antigen-binding fragments thereof is 10 mg/kg or less.

31. The method of claim 1 or 6, wherein the effective amount of one or more of said second antibodies or antigen-binding fragments thereof is 1 mg/kg or less.

32. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of one or more of said second antibodies or antigen-binding fragments thereof.

33. The method of claim 1, 6, 7, or 11, wherein one or more of said second antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of one or more of said first antibodies or antigen-binding fragments thereof.

34. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies or antigen-binding fragments thereof and one or more of said second antibodies or antigen-binding fragments thereof are administered concurrently.

35. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations of one or more of said first antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein one or more of said second antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence.

36. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations of one or more of said second antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein one or more of said first antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence.

37. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies or antigen-binding fragments thereof and one or more of said second antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations are separated by a time period from each other.

38. The method of claim 32, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

39. The method of claim 33, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

40. The method of claim 34, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

41. The method of claim 35, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

42. The method of claim 36, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

43. The method of claim 37, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

44. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies or antigen-binding fragments thereof and/or one or more of said second antibodies or antigen-binding fragments thereof are administered by a nebulizer or an inhaler.

45. The method of claim 1, 6, 7, or 11, wherein one or more of said first antibodies or antigen-binding fragments thereof and/or one or more of said second antibodies or antigen-binding fragments thereof are administered intramuscularly, intravenously or subcutaneously.

46. The method of claim 1 or 6, wherein the viral infection is an infection with RSV and hMPV.

47. The method of claim 1 or 6, wherein the viral infection is an infection with RSV and APV.

48. The method of claim 1, 6, 7, or 11, wherein at least one of said antibodies is a monoclonal antibody, a synthetic antibody, an intrabody, a chimeric antibody, a human antibody, a humanized chimeric antibody, a humanized antibody, a glycosylated antibody, a multispecific antibody, a human antibody, a single-chain antibody, or a bispecific antibody.

49. The method of claim 48, wherein at least one of said antibodies is a human antibody.

50. The method of claim 48, wherein at least one of said antibodies is a humanized antibody.

51. The method of claim 48, wherein at least one of said antibodies is a synthetic antibody.

52. The method of claim 1, 6, 7, or 11, wherein the subject is a mammal.

53. The method of claim 52, wherein the mammal is a primate.

54. The method of claim 53, wherein the primate is a human.

55. The method of claim 54, wherein the human is an elderly human.

56. The method of claim 54, wherein the human is a transplant recipient.

57. The method of claim 54, wherein the human is an immunocompromised patient.

58. The method of claim 54, wherein the human is an AIDS patient.

59. The method of claim 54, wherein the human is an infant.

60. The method of claim 54, wherein the human has cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency, or acquired immunodeficiency or has had a bone marrow transplant.

61. The method of claim 59, wherein the infant was born prematurely or is at risk of hospitalization for a RSV infection and/or for a hMPV infection.

62. The method of claim 59, wherein the human infant was born prematurely.

63. The method of claim 62, wherein the infant was born at 32 weeks of gestational age.

64. The method of claim 62, wherein the infant was born at between 32 and 35 weeks of gestational age.

65. The method of claim 62, wherein the infant was born at more than 35 weeks of gestational age.

66. The method of claim 59, wherein the infant is more than 38 weeks of gestational age.

67. The method of claim 52, wherein the mammal is not a primate.

68. The method of claim 67, wherein the non-primate mammal is an animal model for RSV infection and/or hMPV infection.

69. The method of claim 67, wherein the non-primate mammal is a cotton rat.

70. The method of claim 1, 6, 7, or 11, wherein the antibody is administered once a month just prior to and during the RSV season.

71. The method of claim 1, 6, 7, or 11, wherein the antibody is administered every two months just prior to and during the RSV season.

72. The method of claim 1, 6, 7, or 11, wherein the antibody is administered once just prior to or during the RSV season.

73. The method of claim 1, 6, 7, or 11, wherein at least one of said fragments is a Fab fragment, a F(ab') fragment, a $F(ab')_2$ fragment, a Fd, a single-chain Fv, a disulfide-linked Fv, a fragment comprising a V_L domain, or a fragment comprising a V_H domain.

74. A method of preventing a viral infection in a subject, said method comprising administering to the subject:

(i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein one or more of said antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen.

75. A method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject:

(i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein one or more of said antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen.

76. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein one or more of said antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen,

wherein the dose reduces the incidence of hMPV infection by at least 25%.

77. The method of claim 76, wherein the dose reduces the incidence of hMPV infection by at least 50%.

78. The method of claim 76, wherein the dose reduces the incidence of hMPV infection by at least 75%.

79. The method of claim 76, wherein the dose reduces the incidence of hMPV infection by at least 90%.

80. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a dose of one or more antibodies or antigen-binding fragments thereof, wherein one or more of said antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen,

wherein the serum titer of one or more of said antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said antibodies or antigen-binding fragments thereof.

81. A pharmaceutical composition, said composition comprising:

(i) one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and

(ii) one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen.

82. The pharmaceutical composition of claim 81, wherein the amino acid sequence of the RSV antigen is that of SEQ ID NO:390 to 398, respectively.

83. The pharmaceutical composition of claim 81, wherein the amino acid sequence of the RSV antigen is 90% identical to the amino acid sequence of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, or RSV G protein.

84. The pharmaceutical composition of claim 81, wherein the RSV antigen is selected from the group consisting of RSV nucleoprotein, RSV phosphoprotein, RSV matrix protein, RSV small hydrophobic protein, RSV RNA-dependent RNA polymerase, RSV F protein, and RSV G protein.

85. The pharmaceutical composition of claim 81, wherein one or more of said first antibodies or antigen-binding fragments thereof immunospecifically bind to an antigen of Group A or Group B RSV.

86. The pharmaceutical composition of claim 81, wherein the RSV antigen is RSV F protein.

87. The pharmaceutical composition of claim 81, wherein one or more of said second antibodies cross-react with a turkey APV antigen.

88. The pharmaceutical composition of claim 81, wherein one or more of said second antibodies are (i) human or humanized antibodies and (ii) cross-react with a turkey APV antigen.

89. The pharmaceutical composition of claim 87, wherein said turkey APV antigen is selected from the group consisting of turkey APV nucleoprotein, turkey APV phosphoprotein, turkey APV matrix protein, turkey APV small hydrophobic protein, turkey APV RNA-dependent RNA polymerase, turkey APV F protein, and turkey APV G protein.

90. The pharmaceutical composition of claim 87, wherein said turkey APV antigen is an antigen of avian pneumovirus type A, avian pneumovirus type B, or avian pneumovirus type C.

91. The method of claim 87, wherein the amino acid sequence of said turkey APV antigen is that of SEQ ID NO:424 to 429, respectively.

92. The pharmaceutical composition of claim 81, wherein the amino acid sequence of the hMPV antigen is that of SEQ ID NO: 399-406, 420, or 421, respectively.

93. The pharmaceutical composition of claim 81, wherein the hMPV antigen is selected from the group consisting of hMPV nucleoprotein, hMPV phosphoprotein, hMPV matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and hMPV G protein.

94. The pharmaceutical composition of claim 81, wherein the hMPV antigen is hMPV F protein.

95. The pharmaceutical composition of claim 81, wherein the first antibody is Palivizumab; AFFF; P12f2 P12f4; P11d4; Ale9; A12a6; A13c4; A17d4; A4B4; 1X-493L1; FR H3-3F4; M3H9; Y10H6; DG; AFFF(1); 6H8; L1-7E5; L2-15B10; A13a11; A1h5; A4B4(1);A4B4-F52S; or A4B4L1FR-S28R.

96. The pharmaceutical composition of claim 81, wherein at least one of said antibodies is a monoclonal antibody, a synthetic antibody, an intrabody, a chimeric antibody, a human antibody, a humanized chimeric antibody, a humanized antibody, a glycosylated antibody, a multispecific antibody, a human antibody, a single-chain antibody, or a bispecific antibody.

97. The pharmaceutical composition of claim 96, wherein at least one of said antibodies is a human antibody.

98. The pharmaceutical composition of claim 96, wherein at least one of said antibodies is a humanized antibody.

99. The pharmaceutical composition of claim 96, wherein at least one of said antibodies is a synthetic antibody.

100. The pharmaceutical composition of claim 81, wherein at least one of said fragments is a Fab fragment, a F(ab') fragment, a $F(ab')_2$ fragment, a Fd, a single-chain Fv, a

disulfide-linked Fv, a fragment comprising a V_L domain, or a fragment comprising a V_H domain.

101. A pharmaceutical composition, said composition comprising: one or more antibodies or antigen-binding fragments thereof, wherein one or more of said antibodies or antigen-binding fragments thereof (i) are human or humanized, (ii) cross-react with a turkey APV antigen, and (iii) bind immunospecifically to a hMPV antigen.

102. A method of preventing a viral infection in a subject, said method comprising administering to the subject:

(i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen; and

(ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen.

103. The method of claim 102, wherein one or more of said first antibodies or antigen-binding fragments thereof neutralize PIV.

104. The method of claim 102, wherein one or more of said second antibodies or antigen-binding fragments thereof neutralize hMPV.

105. The method of claim 102, wherein one or more of said first antibodies or antigen-binding fragments thereof block PIV infection of cells of the subject.

106. The method of claim 102, wherein one or more of said second antibodies or antigen-binding fragments thereof block hMPV infection of cells of the subject.

107. A method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject:

(i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen; and

(ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen.

108. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or a fragments thereof bind immunospecifically to a PIV antigen; and

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or a fragments thereof bind immunospecifically to a hMPV antigen,

wherein the first dose reduces the incidence of PIV infection by at least 25% and wherein the second dose reduces the incidence of hMPV infection by at least 25%.

109. The method of claim 108, wherein the first dose reduces the incidence of PIV infection by at least 50% and wherein the second dose reduces the incidence of hMPV infection by at least 50%.

110. The method of claim 108, wherein the first dose reduces the incidence of PIV infection by at least 75% and wherein the second dose reduces the incidence of hMPV infection by at least 75%.

111. The method of claim 108, wherein the first dose reduces the incidence of PIV infection by at least 90% and wherein the second dose reduces the incidence of hMPV infection by at least 90%.

112. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen; and

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen,

wherein the serum titer of one or more of said first antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said first antibodies or antigen-binding fragments thereof and wherein the serum titer of one or more of said second antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said second antibodies or antigen-binding fragments thereof.

113. The method of claim 102, 107, 108, or 112, wherein the amino acid sequence of the PIV antigen is that of SEQ ID NO:407 to 419, respectively.

114. The method of claim 102, 107, 108, or 112, wherein the amino acid sequence of the PIV antigen is 90% identical to the amino acid sequence of PIV nucleocapsid phosphoprotein, PIV L protein, PIV matrix protein, PIV HN glycoprotein, PIV RNA-dependent RNA polymerase, PIV Y1 protein, PIV D protein, or PIV C protein.

115. The method of claim 102, 107, 108, or 112, wherein the PIV antigen is selected from the group consisting of PIV nucleocapsid phosphoprotein, PIV L protein, PIV matrix protein, PIV HN glycoprotein, PIV RNA-dependent RNA polymerase, PIV Y1 protein, PIV D protein, or PIV C protein.

116. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies immunospecifically bind to an antigen of human PIV type 1, human PIV type 2, human PIV type 3, or human PIV type 4.

117. The method of claim 102, 107, 108, or 112, wherein the PIV antigen is PIV F protein.

118. The method of claim 102, 107, 108, or 112, wherein one or more of said second antibodies cross-react with a turkey APV antigen.

119. The method of claim 102, 107, 108, or 112, wherein one or more of said second antibodies are (i) human or humanized antibodies and (ii) cross-react with a turkey APV antigen.

120. The method of claim 118, 119, wherein said turkey APV antigen is selected from the group consisting of turkey APV nucleoprotein, turkey APV phosphoprotein, turkey APV matrix protein, turkey APV small hydrophobic protein, turkey APV RNA-dependent RNA polymerase, turkey APV F protein, and turkey APV G protein.

121. The method of claim 118, 119, wherein said turkey APV antigen is an antigen of avian pneumovirus type A, avian pneumovirus type B, or avian pneumovirus type C.

122. The method of claim 118, 119, wherein the amino acid sequence of said turkey APV antigen is that of SEQ ID NO:424 to 429, respectively.

123. The method of claim 102, 107, 108, or 112, wherein the amino acid sequence of the hMPV antigen is that of SEQ ID NO: 399-406, 420, or 421, respectively.

124. The method of claim 102, 107, 108, or 112, wherein the hMPV antigen is selected from the group consisting of hMPV nucleoprotein, hMPV phosphoprotein, hMPV

matrix protein, hMPV small hydrophobic protein, hMPV RNA-dependent RNA polymerase, hMPV F protein, and hMPV G protein.

125. The method of claim 102, 107, 108, or 112, wherein the hMPV antigen is hMPV F protein.

126. The method of claim 102 or 107, wherein the effective amount of one or more of said first antibodies is 100 mg/kg or less.

127. The method of claim 102 or 107, wherein the effective amount of one or more of said first antibodies is 10 mg/kg or less.

128. The method of claim 102 or 107, wherein the effective amount of one or more of said first antibodies is 1 mg/kg or less.

129. The method of claim 102 or 107, wherein the effective amount of one or more of said second antibodies or antigen-binding fragments thereof is 100 mg/kg or less.

130. The method of claim 102 or 107, wherein the effective amount of one or more of said second antibodies or antigen-binding fragments thereof is 10 mg/kg or less.

131. The method of claim 102 or 107, wherein the effective amount of one or more of said second antibodies or antigen-binding fragments thereof is 1 mg/kg or less.

132. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of one or more of said second antibodies or antigen-binding fragments thereof.

133. The method of claim 102, 107, 108, or 112, wherein one or more of said second antibodies or antigen-binding fragments thereof are administered at a time period prior to administering of one or more of said first antibodies or antigen-binding fragments thereof.

134. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies or antigen-binding fragments thereof and one or more of said second antibodies or antigen-binding fragments thereof are administered concurrently.

135. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations of one or more of said first antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein one or more of said second antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence.

136. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies or antigen-binding fragments thereof are administered in a sequence of two or

more administrations, wherein the administrations of one or more of said second antibodies or antigen-binding fragments thereof are separated by a time period from each other, and wherein one or more of said first antibodies or antigen-binding fragments thereof are administered before, during, or after the sequence.

137. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies or antigen-binding fragments thereof and one or more of said second antibodies or antigen-binding fragments thereof are administered in a sequence of two or more administrations, wherein the administrations are separated by a time period from each other.

138. The method of claim132, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

139. The method of claim 133, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

140. The method of claim 135, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

141. The method of claim 136, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

142. The method of claim 137, wherein the time period is at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, or 3 months.

143. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies or antigen-binding fragments thereof and/or one or more of said second antibodies or antigen-binding fragments thereof are administered by a nebulizer or an inhaler.

144. The method of claim 102, 107, 108, or 112, wherein one or more of said first antibodies or antigen-binding fragments thereof and/or one or more of said second antibodies or antigen-binding fragments thereof are administered intramuscularly, intravenously or subcutaneously.

145. The method of claim 102 or 107, wherein the viral infection is an infection with PIV and hMPV.

146. The method of claim 102 or 107, wherein the viral infection is an infection with PIV and APV.

147. The method of claim 102, 107, 108, or 112, wherein at least one of said antibodies is a monoclonal antibody, a synthetic antibody, an intrabody, a chimeric antibody, a human antibody, a humanized chimeric antibody, a humanized antibody, a glycosylated antibody, a multispecific antibody, a human antibody, a single-chain antibody, or a bispecific antibody.

148. The method of claim 147, wherein at least one of said antibodies is a human antibody.

149. The method of claim 147, wherein at least one of said antibodies is a humanized antibody.

150. The method of claim 147, wherein at least one of said antibodies is a synthetic antibody.

151. The method of claim 102, 107, 108, or 112, wherein the subject is a mammal.

152. The method of claim 151, wherein the mammal is a primate.

153. The method of claim 152, wherein the primate is a human.

154. The method of claim 153, wherein the human is an elderly human.

155. The method of claim 153, wherein the human is a transplant recipient.

156. The method of claim 153, wherein the human is an immunocompromised patient.

157. The method of claim 153, wherein the human is an AIDS patient.

158. The method of claim 153, wherein the human is an infant.

159. The method of claim 153, wherein the human has cystic fibrosis, bronchopulmonary dysplasia, congenital heart disease, congenital immunodeficiency, or acquired immunodeficiency or has had a bone marrow transplant.

160. The method of claim 158, wherein the infant was born prematurely or is at risk of hospitalization for a PIV infection and/or a hMPV infection.

161. The method of claim 158, wherein the infant was born prematurely.

162. The method of claim 161, wherein the infant was born at less than 32 weeks of gestational age.

163. The method of claim 161, wherein the infant was born at 32 and 35 weeks of gestational age.

164. The method of claim 161, wherein the infant was born at 35 weeks of gestational age.

165. The method of claim 158, wherein the infant is more than 38 weeks of gestational age.

166. The method of claim 151, wherein the mammal is not a primate.

167. The method of claim 166, wherein the non-primate mammal is an animal model for PIV infection and/or hMPV infection.

168. The method of claim 166, wherein the non-primate mammal is a cotton rat.

169. The method of claim 102, 107, 108, or 112, wherein the antibody is administered once a month just prior to and during the PIV season.

170. The method of claim 102, 107, 108, or 112, wherein the antibody is administered every two months just prior to and during the PIV season.

171. The method of claim 102, 107, 108, or 112, wherein the antibody is administered once just prior to or during the PIV season.

172. The method of claim 102, 107, 108, or 112, wherein at least one of said fragments is a Fab fragment, a F(ab') fragment, a $F(ab')_2$ fragment, a Fd, a single-chain Fv, a disulfide-linked Fv, a fragment comprising a V_L domain, or a fragment comprising a V_H domain.

173. A method of preventing a viral infection in a subject, said method comprising administering to the subject:

(i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen;

(ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen; and

(iii) a prophylactically effective amount of one or more third antibodies or antigen-binding fragments thereof, wherein one or more of said third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen.

174. The method of claim 173, wherein one or more of said first antibodies or antigen-binding fragments thereof neutralize RSV.

175. The method of claim 173, wherein one or more of said second antibodies or antigen-binding fragments thereof neutralize hMPV.

176. The method of claim 173, wherein one or more of said third antibodies or antigen-binding fragments thereof neutralize PIV.

177. The method of claim 173, wherein one or more of said first antibodies or antigen-binding fragments thereof block RSV infection of cells of the subject.

178. The method of claim 173, wherein one or more of said second antibodies or antigen-binding fragments thereof block hMPV infection of cells of the subject.

179. The method of claim 173, wherein one or more of said third antibodies or antigen-binding fragments thereof block PIV infection of cells of the subject.

180. A method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject:

(i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen;

(ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen; and

(iii) a therapeutically effective amount of one or more third antibodies or antigen-binding fragments thereof, wherein one or more of said third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen.

181. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or a fragments thereof bind immunospecifically to a RSV antigen;

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or a fragments thereof bind immunospecifically to a hMPV antigen; and

(iii) a third dose of one or more third antibodies or antigen-binding fragments thereof, wherein one or more of said third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen.

wherein the first dose reduces the incidence of RSV infection by at least 25%, wherein the second dose reduces the incidence of hMPV infection by at least 25%, and wherein the third dose reduces the incidence of PIV infection by at least 25%.

182. The method of claim 181, wherein the first dose reduces the incidence of RSV infection by at least 50%, wherein the second dose reduces the incidence of hMPV infection by at least 50%, and wherein the third dose reduces the incidence of PIV infection by at least 50%.

183. The method of claim 181, wherein the first dose reduces the incidence of RSV infection by at least 75%, wherein the second dose reduces the incidence of hMPV infection by at least 75%, and wherein the third dose reduces the incidence of PIV infection by at least 75%.

184. The method of claim 181, wherein the first dose reduces the incidence of RSV infection by at least 90%, wherein the second dose reduces the incidence of hMPV infection by at least 90%, and wherein the third antibody reduces the incidence of PIV infection by at least 90%.

185. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen;

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a hMPV antigen; and

(iii) a third dose of one or more third antibodies or antigen-binding fragments thereof, wherein one or more of said third antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen,

wherein the serum titer of one or more of said first antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said first antibodies or antigen-binding fragments thereof, wherein the serum titer of one or more of said second antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said second antibodies or antigen-binding fragments thereof, and wherein the serum titer of one or more of said third antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said third antibodies or antigen-binding fragments thereof.

186. The method of claim 173, 180, 181, or 185, wherein the amino acid sequence of the PIV antigen is that of SEQ ID NO:407 to 419, respectively.

187. The method of claim 173, 180, 181, or 185, wherein the amino acid sequence of the PIV antigen is 90% identical to the amino acid sequence of PIV nucleoprotein, PIV phosphoprotein, PIV matrix protein, PIV small hydrophobic protein, PIV RNA-dependent RNA polymerase, PIV F protein, or PIV G protein.

188. The method of claim 173, 180, 181, or 185, wherein the PIV antigen is selected from the group consisting of PIV nucleoprotein, PIV phosphoprotein, PIV matrix protein, PIV small hydrophobic protein, PIV RNA-dependent RNA polymerase, PIV F protein, and PIV G protein.

189. A method of preventing a viral infection in a subject, said method comprising administering to the subject:

(i) a prophylactically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a prophylactically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen.

190. The method of claim 189 wherein one or more of said first antibodies or antigen-binding fragments thereof neutralize RSV.

191. The method of claim 189, wherein one or more of said second antibodies or antigen-binding fragments thereof neutralize PIV.

192. The method of claim 189, wherein one or more of said first antibodies or antigen-binding fragments thereof block RSV infection of cells of the subject.

193. The method of claim 189, wherein one or more of said second antibodies or antigen-binding fragments thereof block PIV infection of cells of the subject.

194. A method of treating one or more symptoms of a respiratory viral infection in a subject, said method comprising administering to the subject:

(i) a therapeutically effective amount of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a therapeutically effective amount of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen.

195. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or a fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or a fragments thereof bind immunospecifically to a PIV antigen,

wherein the first dose reduces the incidence of RSV infection by at least 25% and wherein the second dose reduces the incidence of PIV infection by at least 25%.

196. The method of claim 195, wherein the first dose reduces the incidence of RSV infection by at least 50% and wherein the second dose reduces the incidence of hMPV infection by at least 50%.

197. The method of claim 195, wherein the first dose reduces the incidence of RSV infection by at least 75% and wherein the second dose reduces the incidence of hMPV infection by at least 75%.

198. The method of claim 195, wherein the first dose reduces the incidence of RSV infection by at least 90% and wherein the second dose reduces the incidence of hMPV infection by at least 90%.

199. A method of passive immunotherapy, said method comprising administering to a subject:

(i) a first dose of one or more first antibodies or antigen-binding fragments thereof, wherein one or more of said first antibodies or antigen-binding fragments thereof bind immunospecifically to a RSV antigen; and

(ii) a second dose of one or more second antibodies or antigen-binding fragments thereof, wherein one or more of said second antibodies or antigen-binding fragments thereof bind immunospecifically to a PIV antigen,

wherein the serum titer of one or more of said first antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said first antibodies or antigen-binding fragments thereof and wherein the serum titer of one or more of said second antibodies or antigen-binding fragments thereof in the subject is at least 10 μg/ml after 15 days of administering one or more of said second antibodies or antigen-binding fragments thereof.

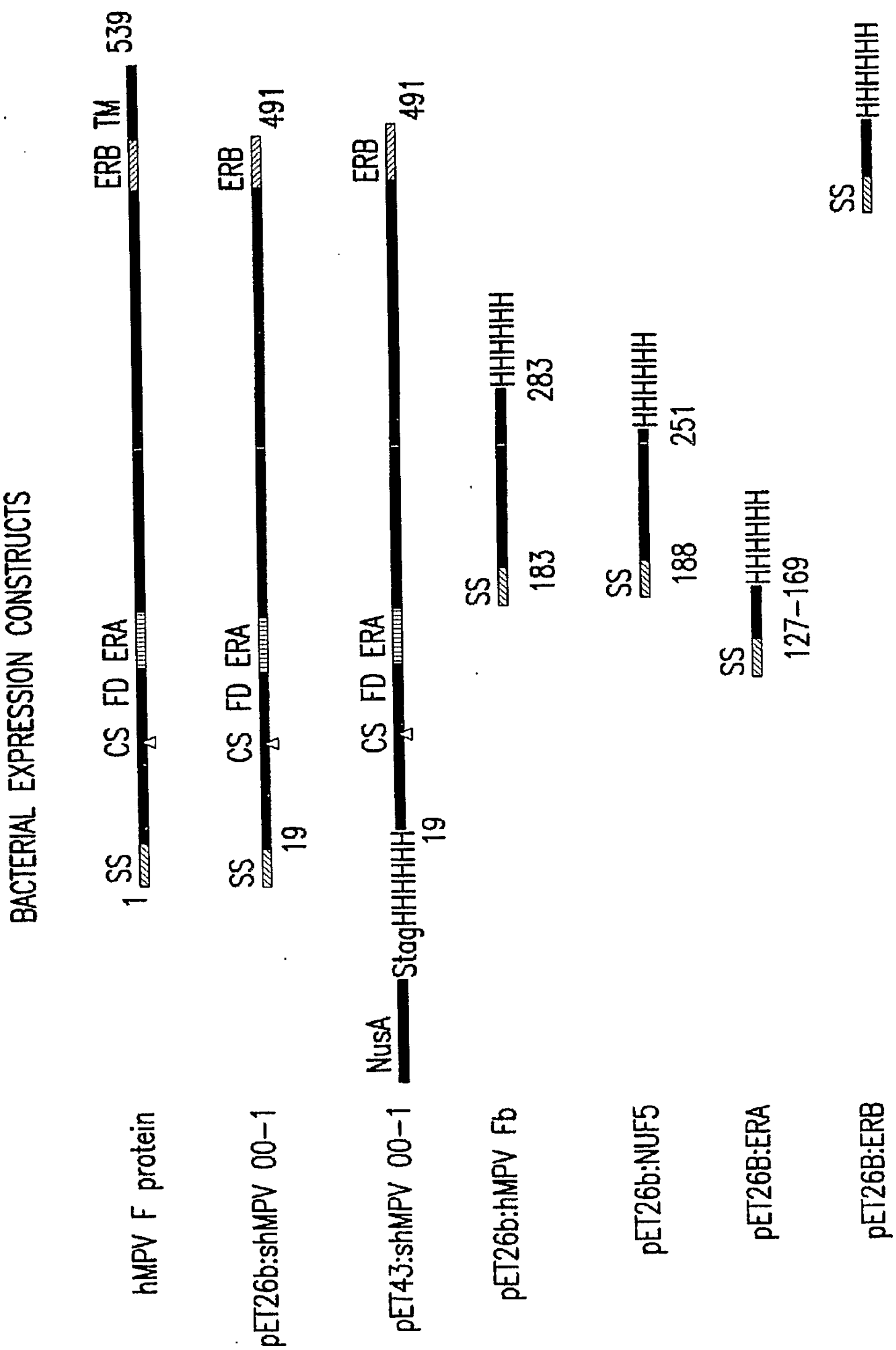
BACTERIAL EXPRESSION CONSTRUCTS
hMPV F protein
1 SS CS FD ERA ERB TM 539
pET26b:shMPV 00-1
SS 19 CS FD ERA ERB 491
pET43:shMPV 00-1
NusA StagHHHHHH 19 CS FD ERA ERB 491
pET26b:hMPV Fb
SS 183 283 HHHHHH
pET26b:NUF5
SS 188 251 HHHHHH
pET26B:ERA
SS 127-169 HHHHHH
pET26B:ERB
SS HHHHHH

FIG.1

SEQUENCE LISTING

<110>MedImmune, Inc.

<120> METHODS OF TREATING AND PREVENTING RSV, HMPV, AND PIV USING ANTI-RSV, ANTI-HMPV, AND ANTI-PIV ANTIBODIES

<130> 10271-072-228

<140> To be assigned
<141> Herewith

<150> 60/398,475
<151> 2002-07-25

<160> 437

<170> FastSEQ for Windows Version 4.0

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<211> 2507
<212> DNA
<213> metapneumovirus

<220>
<221> CDS
<222> (1)...(2507)
<223> Human metapneumovirus isolate 00-1 matrix protein
(M) and fusion protein (F) genes

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ccagcattca tcaaatcagt ttcaatcaaa gagagtgagt cagctactgt tgaagctgct 540
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caagtcatag tagaactagg agcatatgtc caggctgaaa gcataagcaa aatatgcaag 720
acttggagcc atcaagggac aagatatgtc ttgaagtcca gataacaacc aagcaccttg 780
gccaagagct actaacccta tctcatagat cataaagtca ccattctagt tatataaaaa 840
tcaagttaga acaagaatta aatcaatcaa gaacgggaca aataaaaatg tcttggaaag 900
tggtgatcat tttttcattg ttaataacac ctcaacacgg tcttaaagag agctacttag 960
aagagtcatg tagcactata actgaaggat atctcagtgt tctgaggaca ggttggtaca 1020
ccaatgtttt tacactggag gtaggcgatg tagagaacct tacatgtgcc gatggaccca 1080
gcttaataaa aacagaatta gacctgacca aaagtgcact aagagagctc agaacagttt 1140
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tgaaagattt tgtgagcaag aatctaacac gtgcaatcaa caaaaacaag tgcgacattg 1440
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ggcaattttc agacaacgct ggaataacac cagcaatatc tttggactta atgacagatg 1560
ctgaactagc cagagctgtt tccaacatgc caacatctgc aggacaaata aaactgatgt 1620
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aagaccaagg atggtattgt caaaatgcag ggtcaactgt ttactaccca aatgaaaaag 1860
actgtgaaac aagaggagac catgtctttt gcgacacagc agcaggaatc aatgttgctg 1920
agcagtcaaa ggagtgcaac ataaacatat ctactactaa ttacccatgc aaagttagca 1980
caggaagaca tcctatcagt atggttgcac tatctcctct tggggctttg gttgcttgct 2040
acaagggagt gagctgttcc attggcagca acagagtagg gatcatcaag caactgaaca 2100
aaggctgctc ttatataacc aaccaagacg cagacacagt gacaatagac aacactgtat 2160
accagctaag caaagttgaa ggcgaacagc atgttataaa aggaaggcca gtgtcaagca 2220
gctttgaccc agtcaagttt cctgaagatc aattcaatgt tgcacttgac caagttttcg 2280
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agaaaggaaa cactggcttc atcattgtaa taattctaat tgctgtcctt ggctctacca 2400
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<212> DNA
<213> pneumvirus

<220>
<221> CDS
<222> (1)...(1596)
<223> Avian pneumovirus fusion protein gene, partial cds

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gaaagttatc tagaggagtc atgcagtact gttactagag gatacctgag tgttttgagg 120
acaggatggt atacaaatgt gttcacactt ggggttggag atgtgaaaaa tctcacatgt 180
accgacgggc ccagcttaat aagaacagaa cttgaactga caaaaaatgc acttgaggaa 240
ctcaagacag tatcagcaga tcaattggca aaggaagcta ggataatgtc accaagaaaa 300
gcccggtttg ttctgggtgc catagcatta ggtgtggcaa ctgctgctgc tgtgacggct 360
ggtgtagcga tagccaagac aattaggcta gaaggagaag tggctgcaat caaaggtgcg 420
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gctgtgaatg atctcaagga ctttataagt aaaaaattga cacctgcaat aaacaggaac 540
aagtgtgaca tctcagacct taagatggca gtgagctttg gacaatacaa tcggaggttc 600
ctcaatgtgg taagacagtt ttctgacaat gcaggtatta cgcctgcaat atctctagat 660
ttaatgactg acgctgagct tgtaagagct gtaagcaaca tgcccacatc ttcaggacag 720
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acaccgtgtt ggagggtgaa ggctgctcca ttatgttcag ggaaagacgg gaattatgca 900
tgtctcttgc gagaggacca aggttggtat tgtcaaaatg ctggatccac agtttattat 960
ccaaatgagg aggactgtga agtaagaagt gatcatgtgt tttgtgacac agcagctggg 1020
ataaatgtag caaaggagtc agaagagtgc aacaggaata tctcaacaac aaagtaccct 1080
tgcaaggtaa gtacagggcg tcacccaata agcatggtgg ccttatcacc actgggtgct 1140
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agacctttgg ggaaagggtg ttcatacatc agcaatcaag atgctgacac tgttacaatt 1260
gacaacacag tgtaccaatt gagcaaagtt gaaggagaac aacacacaat taaagggaag 1320
ccagtatcta gcaattttga ccctatagag ttccctgaag atcagttcaa cgtagccctg 1380
gatcaggtgt ttgaaagtgt tgagaagagt cagaatctga tagaccagtc aaacaagata 1440
ttggatagca ttgaaaaggg gaatgcagga tttgtcatag tgatagtcct cattgtcctg 1500
ctcatgctgg cagcagttgg tgtgggtgtc ttctttgtgg ttaagaagag aaaagctgct 1560
cccaaattcc caatggaaat gaatggtgtg aacaac 1596

<210> 3
<211> 1666
<212> DNA
<213> pneumovirus

<220>
<221> CDS
<222> (14)...(1627)

<223> Avian pneumovirus isolate 1b fusion protein mRNA,
complete cds

<400> 3
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ggggggggcta gaagaaagtt atctagagga gtcatgcagt actgttacta gaggatacct 120
gagtgttttg aggacaggat ggtatacaaa tgtgttcaca cttgaggttg gagatgtgga 180
aaatctcaca tgtaccgacg ggcccagctt aataagaaca gaacttgaac tgacaaaaaa 240
tgcacttgag gaactcaaga cagtatcagc agatcaattg gcaaaggaag ctaggataat 300
gtcaccaaga aaagcccggt ttgttctggg tgccatagca ttaggtgtgg caactgctgc 360
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aatcaagggt gcgctcagga aaacaaatga ggctgtatct acattaggaa atggcgtgag 480
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cctcattgtc ctgctcatgc tggcagcagt tggtgtgggt gtcttctttg tggttaagaa 1560
gagaaaagct gctcccaaat tcccaatgga aatgaatggt gtgaacaaca aaggatttat 1620
cccttaattt tagttattaa aaaaaaaaaa aaaaaaaaaa aaaaaa 1666

<210> 4
<211> 1636
<212> DNA
<213> rhinotracheitis virus

<220>
<221> CDS
<222> (13)...(1629)
<223> Turkey rhinotracheitis virus gene for fusion
protein (F1 and F2 subunits), complete cds

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agtgtgttaa ggacagggtg gtatacgaat gtatttaacc tcgaaatagg gaatgttgag 180
aacatcactt gcaatgatgg acccagccta attgacactg agttagtact cacaaagaat 240
gctttgaggg agctcaaaac agtgtcagct gatcaagtgg ctaaggaaag cagactatcc 300
tcacccagga gacgtagatt tgtactgggt gcaatagcac ttggtgttgc gacagctgct 360
gccgtaacag ctggtgtagc acttgcaaag acaattagat tagagggaga ggtgaaggca 420
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aacagaaggt tcctgaatgt ggtgaggcaa ttctctgata gtgcaggtat cacatcagct 660
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gtcagttaag ttattt 1636

<210> 5
<211> 1860
<212> DNA
<213> pneumovirus

<220>
<221> CDS
<222> (1)...(110)
<223> Avian pneumovirus matrix protein (M) gene, partial
cds

<220>
<221> CDS
<222> (216)...(1829)
<223> Avian pneumovirus fusion glycoprotein (F) gene,
complete cds

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gcaggaactg gagccaccag ggtacgagat atgtcctgaa gtcaagataa acacagagag 120
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<212> PRT
<213> paramyxovirus

<220>
<223> paramyxovirus F protein hRSV B

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Ile Asn Ala Leu Tyr Leu Thr Ser Ser Gln Asn Ile Thr Glu Glu Phe
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Tyr Gln Ser Thr Cys Ser Ala Val Ser Arg Gly Tyr Phe Ser Ala Leu
35 40 45
Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60
Lys Glu Thr Lys Cys Asn Gly Thr Asp Thr Lys Val Lys Leu Ile Lys
65 70 75 80
Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95
Met Gln Asn Thr Pro Ala Ala Asn Asn Arg Ala Arg Arg Glu Ala Pro
100 105 110
Gln Tyr Met Asn Tyr Thr Ile Asn Thr Thr Lys Asn Leu Asn Val Ser
115 120 125
Ile Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140
Gly Ser Ala Ile Ala Ser Gly Ile Ala Val Ser Lys Val Leu His Leu
145 150 155 160
Glu Gly Glu Val Asn Lys Ile Lys Asn Ala Leu Leu Ser Thr Asn Lys
165 170 175
Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190
Leu Asp Leu Lys Asn Tyr Ile Asn Asn Gln Leu Leu Pro Ile Val Asn
195 200 205
Gln Gln Ser Cys Arg Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220
Gln Lys Asn Ser Arg Leu Leu Glu Ile Asn Arg Glu Phe Ser Val Asn
225 230 235 240
Ala Gly Val Thr Thr Pro Leu Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255
Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270
Leu Met Ser Ser Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285
Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300
Ile Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320
Leu Cys Thr Thr Asn Ile Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335
Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350
Pro Gln Ala Asp Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
355 360 365
Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Ser Leu Cys Asn Thr
370 375 380
Asp Ile Phe Asn Ser Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr

385 390 395 400
Asp Ile Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415
Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445
Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Leu Glu Gly
450 455 460
Lys Asn Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Tyr Tyr Asp Pro
465 470 475 480
Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495
Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Arg Ser Asp Glu Leu
500 505 510
Leu His Asn Val Asn Thr Gly Lys Ser Thr Thr Asn Ile Met Ile Thr
515 520 525
Thr Ile Ile Ile Val Ile Ile Val Val Leu Leu Ser Leu Ile Ala Ile
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Gly Leu Leu Leu Tyr Cys Lys Ala Lys Asn Thr Pro Val Thr Leu Ser
545 550 555 560
Lys Asp Gln Leu Ser Gly Ile Asn Asn Ile Ala Phe Ser Lys
565 570

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<212> PRT
<213> paramyxovirus

<220>
<223> paramyxovirus F protein hRSV A2

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Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45
Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60
Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80
Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95
Met Gln Ser Thr Pro Pro Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110
Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125
Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140
Gly Ser Ala Ile Ala Ser Gly Val Ala Val Ser Lys Val Leu His Leu
145 150 155 160
Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
165 170 175
Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190
Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
195 200 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220
Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240
Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255
Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270
Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285
Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300
Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320
Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335
Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350
Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
355 360 365
Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Ile Asn Leu Cys Asn Val
370 375 380
Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400
Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415
Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430
Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Met Asp
435 440 445
Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
450 455 460
Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465 470 475 480
Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495
Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
500 505 510
Leu His Asn Val Asn Ala Gly Lys Ser Thr Thr Asn Ile Met Ile Thr
515 520 525
Thr Ile Ile Ile Val Ile Ile Val Ile Leu Leu Ser Leu Ile Ala Val
530 535 540
Gly Leu Leu Leu Tyr Cys Lys Ala Arg Ser Thr Pro Val Thr Leu Ser
545 550 555 560
Lys Asp Gln Leu Ser Gly Ile Asn Asn Ile Ala Phe Ser Asn
565 570

<210> 8
<211> 121
<212> PRT
<213> metapneumovirus

<220>
<223> human metapneumovirus01-71 (partial sequence)

<400> 8
Leu Leu Ile Thr Pro Gln His Gly Leu Lys Glu Ser Tyr Leu Glu Glu
1 5 10 15
Ser Cys Ser Thr Ile Thr Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly
20 25 30

Trp Tyr Thr Asn Val Phe Thr Leu Glu Val Gly Asp Val Glu Asn Leu
35 40 45

Thr Cys Ala Asp Gly Pro Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr
50 55 60
Lys Ser Ala Leu Arg Glu Leu Arg Thr Val Ser Ala Asp Gln Leu Ala
65 70 75 80
Arg Glu Glu Gln Ile Glu Asn Pro Arg Gln Ser Arg Phe Val Leu Gly
85 90 95
Ala Ile Ala Leu Gly Val Ala Thr Ala Ala Ala Val Thr Ala Gly Val
100 105 110
Ala Ile Ala Lys Thr Ile Arg Leu Glu
115 120

<210> 9
<211> 539
<212> PRT
<213> metapneumovirus

<220>
<223> Human metapneumovirus isolate 00-1 matrix protein
(M) and fusion protein (F) genes

<400> 9
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1 5 10 15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ala Asp Gly Pro
50 55 60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80
Leu Arg Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85 90 95
Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Lys Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
165 170 175
Ile Asn Lys Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225 230 235 240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Phe Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
275 280 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
340 345 350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385 390 395 400
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
435 440 445
Val Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465 470 475 480
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
485 490 495
Leu Ile Ala Val Leu Gly Ser Thr Met Ile Leu Val Ser Val Phe Ile
500 505 510
Ile Ile Lys Lys Thr Lys Arg Pro Thr Gly Ala Pro Pro Glu Leu Ser
515 520 525
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
530 535

<210> 10
<211> 532
<212> PRT
<213> Avian pneumovirus

<220>
<223> Avian pneumovirus fusion protein gene, partial cds

<400> 10
Met Ser Trp Lys Val Val Leu Leu Leu Val Leu Leu Ala Thr Pro Thr
1 5 10 15
Gly Gly Leu Glu Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Val Thr
20 25 30
Arg Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Gly Val Gly Asp Val Lys Asn Leu Thr Cys Thr Asp Gly Pro
50 55 60
Ser Leu Ile Arg Thr Glu Leu Glu Leu Thr Lys Asn Ala Leu Glu Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Lys Glu Ala Arg Ile Met
85 90 95
Ser Pro Arg Lys Ala Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Gly Glu Val Ala Ala Ile Lys Gly Ala Leu Arg Lys Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr

145 150 155 160
Ala Val Asn Asp Leu Lys Asp Phe Ile Ser Lys Lys Leu Thr Pro Ala
165 170 175
Ile Asn Arg Asn Lys Cys Asp Ile Ser Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Gly Gln Tyr Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Val Arg Ala Val Ser Asn Met Pro Thr Ser Ser Gly Gln
225 230 235 240
Ile Asn Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Val Tyr Ile Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Arg Val Lys Ala
275 280 285
Ala Pro Leu Cys Ser Gly Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Glu Asp Cys Glu Val Arg Ser Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Lys Glu Ser Glu Glu Cys Asn Arg
340 345 350
Asn Ile Ser Thr Thr Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Asp Gly Met Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385 390 395 400
Arg Pro Leu Gly Lys Gly Cys Ser Tyr Ile Ser Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Thr Ile Lys Gly Lys Pro Val Ser Ser Asn Phe Asp Pro
435 440 445
Ile Glu Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Val Glu Lys Ser Gln Asn Leu Ile Asp Gln Ser Asn Lys Ile
465 470 475 480
Leu Asp Ser Ile Glu Lys Gly Asn Ala Gly Phe Val Ile Val Ile Val
485 490 495
Leu Ile Val Leu Leu Met Leu Ala Ala Val Gly Val Gly Val Phe Phe
500 505 510
Val Val Lys Lys Arg Lys Ala Ala Pro Lys Phe Pro Met Glu Met Asn
515 520 525
Gly Val Asn Asn
530

<210> 11
<211> 537
<212> PRT
<213> Avian pneumovirus

<220>
<223> Avian pneumovirus isolate 1b fusion protein mRNA,
complete cds

<400> 11
Met Ser Trp Lys Val Val Leu Leu Leu Val Leu Leu Ala Thr Pro Thr

1 5 10 15
Gly Gly Leu Glu Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Val Thr
20 25 30
Arg Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
50 55 60
Ser Leu Ile Arg Thr Glu Leu Glu Leu Thr Lys Asn Ala Leu Glu Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Lys Glu Ala Arg Ile Met
85 90 95
Ser Pro Arg Lys Ala Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110

Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Gly Glu Val Ala Ala Ile Lys Gly Ala Leu Arg Lys Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160
Ala Val Asn Asp Leu Lys Asp Phe Ile Ser Lys Lys Leu Thr Pro Ala
165 170 175
Ile Asn Arg Asn Lys Cys Asp Ile Ser Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Gly Gln Tyr Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Val Arg Ala Val Ser Asn Met Pro Thr Ser Ser Gly Gln
225 230 235 240
Ile Asn Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Val Tyr Ile Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Lys Val Lys Ala
275 280 285
Ala Pro Leu Cys Ser Gly Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Glu Asp Cys Glu Val Arg Ser Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Lys Glu Ser Glu Glu Cys Asn Arg
340 345 350
Asn Ile Ser Thr Thr Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Asp Gly Met Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385 390 395 400
Arg Pro Leu Gly Lys Gly Cys Ser Tyr Ile Ser Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Thr Ile Lys Gly Lys Pro Val Ser Ser Asn Phe Asp Pro
435 440 445
Ile Glu Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Val Glu Lys Ser Gln Asn Leu Ile Asp Gln Ser Asn Lys Ile
465 470 475 480
Leu Asp Ser Ile Glu Lys Gly Asn Ala Gly Phe Val Ile Val Ile Val

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                    485                                     490                                     495
Leu Ile Val Leu Leu Met Leu Ala Ala Val Gly Val Gly Val Phe Phe
                500                                     505                                     510
Val Val Lys Lys Arg Lys Ala Ala Pro Lys Phe Pro Met Glu Met Asn
        515                                     520                                     525
Gly Val Asn Asn Lys Gly Phe Ile Pro
    530                                     535

<210> 12
<211> 538
<212> PRT
<213> Turkey rhinotracheitis virus

<220>
<223> Turkey rhinotracheitis virus gene for fusion
      protein (F1 and F2 subunits), complete cds

<400> 12
Met Asp Val Arg Ile Cys Leu Leu Leu Phe Leu Ile Ser Asn Pro Ser
1               5                   10                  15
Ser Cys Ile Gln Glu Thr Tyr Asn Glu Glu Ser Cys Ser Thr Val Thr
            20                  25                  30
Arg Gly Tyr Lys Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45
Asn Leu Glu Ile Gly Asn Val Glu Asn Ile Thr Cys Asn Asp Gly Pro
    50                  55                  60
Ser Leu Ile Asp Thr Glu Leu Val Leu Thr Lys Asn Ala Leu Arg Glu
65                  70                  75                  80
Leu Lys Thr Val Ser Ala Asp Gln Val Ala Lys Glu Ser Arg Leu Ser
                85                  90                  95
Ser Pro Arg Arg Arg Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Leu Ala Lys Thr Ile
        115                 120                 125
Arg Leu Glu Gly Glu Val Lys Ala Ile Lys Asn Ala Leu Arg Asn Thr
    130                 135                 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160
Ala Val Asn Asp Leu Lys Glu Phe Ile Ser Lys Lys Leu Thr Pro Ala
                165                 170                 175
Ile Asn Gln Asn Lys Cys Asn Ile Ala Asp Ile Lys Met Ala Ile Ser
            180                 185                 190
Phe Gly Gln Asn Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205
Asp Ser Ala Gly Ile Thr Ser Ala Val Ser Leu Asp Leu Met Thr Asp
    210                 215                 220
Asp Glu Leu Val Arg Ala Ile Asn Arg Met Pro Thr Ser Ser Gly Gln
225                 230                 235                 240
Ile Ser Leu Met Leu Asn Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255
Gly Ile Leu Ile Gly Val Tyr Asp Gly Thr Val Val Tyr Met Val Gln
            260                 265                 270
Leu Pro Ile Phe Gly Val Ile Glu Thr Pro Cys Trp Arg Val Val Ala
        275                 280                 285
Ala Pro Leu Cys Arg Lys Glu Lys Gly Asn Tyr Ala Cys Ile Leu Arg
    290                 295                 300
Glu Asp Gln Gly Trp Tyr Cys Thr Asn Ala Gly Ser Thr Ala Tyr Tyr
305                 310                 315                 320
Pro Asn Lys Asp Asp Cys Glu Val Arg Asp Asp Tyr Val Phe Cys Asp
                325                 330                 335
Thr Ala Ala Gly Ile Asn Val Ala Leu Glu Val Glu Gln Cys Asn Tyr
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                340                      345                      350
Asn Ile Ser Thr Ser Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
            355                     360                     365
Pro Val Ser Met Val Ala Leu Thr Pro Leu Gly Gly Leu Val Ser Cys
    370                     375                     380
Tyr Glu Ser Val Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385                     390                     395                     400
Lys Gln Leu Gly Lys Gly Cys Thr His Ile Pro Asn Asn Glu Ala Asp
                405                     410                     415
Thr Ile Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Val Gly
                420                     425                     430
Glu Gln Arg Thr Ile Lys Gly Ala Pro Val Val Asn Asn Phe Asn Pro
            435                     440                     445
Ile Leu Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                     455                     460

Glu Ser Ile Asp Arg Ser Gln Asp Leu Ile Asp Lys Ser Asn Asp Leu
465                     470                     475                     480
Leu Gly Ala Asp Ala Lys Ser Lys Ala Gly Ile Ala Ile Ala Ile Val
                485                     490                     495
Val Leu Val Ile Leu Gly Ile Phe Phe Leu Leu Ala Val Ile Tyr Tyr
                500                     505                     510
Cys Ser Arg Val Arg Lys Thr Lys Pro Lys His Asp Tyr Pro Ala Thr
            515                     520                     525
Thr Gly His Ser Ser Met Ala Tyr Val Ser
    530                     535

<210> 13
<211> 537
<212> PRT
<213> Avian penumovirus

<220>
<223> Avian pneumovirus fusion glycoprotein (F) gene,
      complete cds

<400> 13
Met Ser Trp Lys Val Val Leu Leu Leu Val Leu Leu Ala Thr Pro Thr
1               5                   10                  15
Gly Gly Leu Glu Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Val Thr
            20                  25                  30
Arg Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
    50                  55                  60
Ser Leu Ile Arg Thr Glu Leu Glu Leu Thr Lys Asn Ala Leu Glu Glu
65                  70                  75                  80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Lys Glu Ala Arg Ile Met
                85                  90                  95
Ser Pro Arg Lys Ala Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125
Arg Leu Glu Gly Glu Val Ala Ala Ile Lys Gly Ala Leu Arg Lys Thr
    130                 135                 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160
Ala Val Asn Asp Leu Lys Asp Phe Ile Ser Lys Lys Leu Thr Pro Ala
                165                 170                 175
Ile Asn Arg Asn Lys Cys Asp Ile Ser Asp Leu Lys Met Ala Val Ser
            180                 185                 190
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Phe Gly Gln Tyr Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Val Arg Ala Val Ser Asn Met Pro Thr Ser Ser Gly Gln
225 230 235 240
Ile Asn Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Val Tyr Ile Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Lys Val Lys Ala
275 280 285
Ala Pro Leu Cys Ser Gly Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320

Pro Asn Glu Glu Asp Cys Glu Val Arg Ser Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Lys Glu Ser Glu Glu Cys Asn Arg
340 345 350
Asn Ile Ser Thr Thr Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Asp Gly Met Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385 390 395 400
Arg Pro Leu Gly Lys Gly Cys Ser Tyr Ile Ser Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Thr Ile Lys Gly Lys Pro Val Ser Ser Asn Phe Asp Pro
435 440 445
Ile Glu Phe Pro Glu Asp Gln Phe Asn Ile Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Val Glu Lys Ser Gln Asn Leu Ile Asp Gln Ser Asn Lys Ile
465 470 475 480
Leu Asp Ser Ile Glu Lys Gly Asn Ala Gly Phe Val Ile Val Ile Val
485 490 495
Leu Ile Val Leu Leu Met Leu Ala Ala Val Gly Val Gly Val Phe Phe
500 505 510
Val Val Lys Lys Arg Lys Ala Ala Pro Lys Phe Pro Met Glu Met Asn
515 520 525
Gly Val Asn Asn Lys Gly Phe Ile Pro
530 535

<210> 14
<211> 1193
<212> DNA
<213> rhinotracheitis virus

<220>
<221> CDS
<222> (16)...(1191)
<223> Turkey rhinotracheitis virus (strain CVL14/1)
attachment protien (G) mRNA, complete cds

<400> 14
gggacaagta tctctatggg gtccaaacta tatatggctc agggcaccag tgcatatcaa 60
actgcagtgg ggttctggct ggacatcggg aggaggtaca tattggctat agtcctatca 120
gctttcgggc tgacctgcac agtcactatt gcactcactg ttagcgtcat agttgaacag 180

tcagtgttag aggagtgcag aaactacaat ggaggagata gagattggtg gtcaaccacc 240
caggagcagc caactactgc accaagtgcg actccagcag gaaattatgg aggattacaa 300
acggctcgaa caagaaagtc tgaaagctgt ttgcatgtgc aaatttctta tggtgatatg 360
tatagccgca gtgatactgt actgggtggt tttgattgta tgggcttatt ggttctttgc 420
aaatcaggac caatttgtca gcgagataat caagttgacc caacagccct ctgccattgc 480
agggtagatc tttcaagtgt ggactgctgc aaggtgaaca agattagcac taacagcagc 540
accacctctg agccccagaa gaccaacccg gcatggccta gccaagacaa cacagactcc 600
gatccaaatc cccaaggcat aaccaccagc acagccactc tgctctcaac aagtctgggc 660
ctcatgctca catcgaagac tgggacacac aaatcagggc ccccccaagc cttgccgggg 720
agcaacacca acggaaaaac aaccacagac cgagaaccag ggcccacaaa ccaaccaaat 780
tcaaccacca atgggcaaca caataaacac acccaacgaa tgacaccccc gccaagtcac 840
gacaacacaa gaaccatcct ccagcacaca acaccctggg aaaagacatt cagtacatac 900
aagcccacac actctccgac caacgaatca gatcaatccc tccccacaac tcaaaacagc 960
atcaactgtg aacattttga cccccaaggc aaggaaaaaa tctgctacag agtaggttct 1020
tacaactcca atattacaaa gcaatgcaga attgatgtgc ctttgtgttc cacttatagc 1080
acagtgtgca tgaaaacata ctataccgaa ccattcaact gttggaggcg tatctggcgt 1140
tgcttgtgtg atgacggagt tggtctggtt gagtggtgtt gcactagtta act 1193

<210> 15
<211> 1260
<212> DNA
<213> rhinotracheitis virus

<220>
<221> CDS
<222> (16)...(1260)
<223> Turkey rhinotracheitis virus (strain 6574)
attachment protein (G), complete cds

<400> 15
gggacaagta tccagatggg gtcagagctc tacatcatag agggggtgag ctcatctgaa 60
atagtcctca agcaagtcct cagaaggagc caaaaaatac tgttaggact ggtgttatca 120
gccttaggct tgacgctcac tagcactatt gttatatcta tttgtattag tgtagaacag 180
gtcaaattac gacagtgtgt ggacacttat tgggcggaaa atggatcctt acatccagga 240
cagtcaacag aaaatacttc aacaagaggt aagactacaa caaaagaccc tagaagatta 300
caggcgactg gagcaggaaa gtttgagagc tgtgggtatg tgcaagttgt tgatggtgat 360
atgcatgatc gcagttatgc tgtactgggt ggtgttgatt gtttgggctt attggctctt 420
tgtgaatcag gaccaatttg tcagggagat acttggtctg aagacggaaa cttctgccga 480
tgcacttttt cttcccatgg ggtgagttgc tgcaaaaaac ccaaaagcaa ggcaaccact 540
gcccagagga actccaaacc agctaacagc aaatcaactc ctccggtaca ttcagacagg 600
gccagcaaag aacataatcc ctcccaaggg gagcaacccc gcagggggcc aaccagcagc 660
aagacaacta ttgctagcac cccttcaaca gaggacactg ctaaaccaac gattagcaaa 720
cctaaactca ccatcaggcc ctcgcaaaga ggtccatccg gcagcacaaa agcagcctcc 780
agcaccccca gccacaagac caacaccaga ggcaccagca agacgaccga ccagagaccc 840
cgcaccggac ccactcccga aaggcccaga caaacccaca gcacagcaac tccgcccccc 900
acaaccccaa tccacaaggg ccgggcccca acccccaaac caacaacaga cctcaaggtc 960
aacccaaggg aaggcagcac aagcccaact gcaatacaga aaaacccaac cacacaaagt 1020
aatcttgttg actgcacact gtctgatcca gatgagccac aaaggatttg ttaccaggta 1080
ggaacttaca atcctagtca atcgggaacc tgcaacatag aggttccaaa atgttccact 1140
tatgggcatg cttgtatggc tacattatat gacaccccat tcaactgctg gcgcaggacc 1200
aggagatgca tctgtgattc cggaggggag ctgattgagt ggtgctgtac tagtcaataa 1260

<210> 16
<211> 391
<212> PRT
<213> Turkey rhinotracheitis virus

<220>
<223> Turkey rhinotracheitis virus (strain CVL14/1)
attachment protien (G) mRNA, complete cds

<400> 16

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Met Gly Ser Lys Leu Tyr Met Ala Gln Gly Thr Ser Ala Tyr Gln Thr
1               5                   10                  15
Ala Val Gly Phe Trp Leu Asp Ile Gly Arg Arg Tyr Ile Leu Ala Ile
            20                  25                  30
Val Leu Ser Ala Phe Gly Leu Thr Cys Thr Val Thr Ile Ala Leu Thr
        35                  40                  45
Val Ser Val Ile Val Glu Gln Ser Val Leu Glu Glu Cys Arg Asn Tyr
    50                  55                  60
Asn Gly Gly Asp Arg Asp Trp Trp Ser Thr Thr Gln Glu Gln Pro Thr
65                  70                  75                  80
Thr Ala Pro Ser Ala Thr Pro Ala Gly Asn Tyr Gly Gly Leu Gln Thr
                85                  90                  95
Ala Arg Thr Arg Lys Ser Glu Ser Cys Leu His Val Gln Ile Ser Tyr
            100                 105                 110
Gly Asp Met Tyr Ser Arg Ser Asp Thr Val Leu Gly Gly Phe Asp Cys
        115                 120                 125
Met Gly Leu Leu Val Leu Cys Lys Ser Gly Pro Ile Cys Gln Arg Asp
    130                 135                 140
Asn Gln Val Asp Pro Thr Ala Leu Cys His Cys Arg Val Asp Leu Ser
145                 150                 155                 160
Ser Val Asp Cys Cys Lys Val Asn Lys Ile Ser Thr Asn Ser Ser Thr
                165                 170                 175
Thr Ser Glu Pro Gln Lys Thr Asn Pro Ala Trp Pro Ser Gln Asp Asn
            180                 185                 190
Thr Asp Ser Asp Pro Asn Pro Gln Gly Ile Thr Thr Ser Thr Ala Thr
        195                 200                 205
Leu Leu Ser Thr Ser Leu Gly Leu Met Leu Thr Ser Lys Thr Gly Thr
    210                 215                 220
His Lys Ser Gly Pro Pro Gln Ala Leu Pro Gly Ser Asn Thr Asn Gly
225                 230                 235                 240
Lys Thr Thr Thr Asp Arg Glu Pro Gly Pro Thr Asn Gln Pro Asn Ser
                245                 250                 255
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Pro Ser His Asp Asn Thr Arg Thr Ile Leu Gln His Thr Thr Pro Trp
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Phe Asp Pro Gln Gly Lys Glu Lys Ile Cys Tyr Arg Val Gly Ser Tyr
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Cys Leu Gly Leu Leu Ala Leu Cys Glu Ser Gly Pro Ile Cys Gln Gly
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catgcccact ataaaaggtc ag 22

<210> 35
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 35
caccccagtc tttcttgaaa 20

<210> 36
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 36
tgcttgtact tcccaaag 18

<210> 37
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 37
tatttgaaca aaaagtgt 18

<210> 38
<211> 19

<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 38
tggtgtggga tattaacag 19

<210> 39
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 39
aagcccaaaa gctggactgt ttagccaact gtcccaactt tgcaaggttc tcggaaatgc 60
ctcagg 66

<210> 40
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 40
aagcccaaaa gctggactgt ttagccaact gtcctaactt tgcaaggttc tcggaaatgc 60
ctcagg 66

<210> 41
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 41
aagcccaaaa gctggactgt ttagccaatt gtcccaactt tgcaaggttc tcggcaatgc 60
ctcagg 66

<210> 42
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 42
aagcccaaaa gctggattgt ttagccaatt gtcccaactt tgcaaggttc tcggcaatgc 60
ctcagg 66

<210> 43
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 43
aagcccaaaa gctggactgt ttagccaatt gtcccaactt tgctaggttc tcggcaatgc 60
ctcagg 66

<210> 44
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 44
aagtccaaag gcagggctgt ttggccaatt gccccaattt tgctaggttc ttggcaatgc 60
ttcagg 66

<210> 45
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 45
aagtccaaag gcagggctgt ttggccaatt gccccaattt tgctaggttc ttggcaatgc 60
ttcagg 66

<210> 46
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 46
cccaccacca gagagaaa 18

<210> 47
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 47
accaccagag agaaaccc 18

<210> 48
<211> 18
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<220>
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<400> 48
accagagaga aacccacc 18

<210> 49
<211> 18
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<220>
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<400> 49
agagagaaac ccaccacc 18

<210> 50
<211> 18
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<213> Artificial Sequence

<220>
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<400> 50
gagaaaccca ccaccaga 18

<210> 51
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 51
aaacccacca ccagagag 18

<210> 52
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 52
ggaggcaagc gaacgcaa 18

<210> 53
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 53
ggcaagcgaa cgcaagga 18

<210> 54
<211> 18

<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 54
aagcgaacgc aaggaggc 18

<210> 55
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 55
cgaacgcaag gaggcaag 18

<210> 56
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 56
acgcaaggag gcaagcga 18

<210> 57
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 57
caaggaggca agcgaacg 18

<210> 58
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 58
tgttgtcgag actattccaa 20

<210> 59
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 59
tgttgwacca gttgcagtct 20

<210> 60
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 60
tgctgcttct attgagaaac gcc 23

<210> 61
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 61
ggtgacttcy aatagggcca 20

<210> 62
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 62
ctcgaggttg tcaggatata g 21

<210> 63
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 63
ctttgggagt tgaacacagt t 21

<210> 64
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 64
ttcrgtttta gctgcttacg 20

<210> 65
<211> 21
<212> DNA

<213> Artificial Sequence

<220>
<223> Primer

<400> 65
aggcaaatct ctggataatg c 21

<210> 66
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 66
tcgtaacgtc tcgtgacc 18

<210> 67
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 67
ggagatcttt ctagagtgag 20

<210> 68
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<220>
<221> misc_feature
<222> 10, 19
<223> n = A,T,C or G

<220>
<221> misc_feature
<222> 10, 19
<223> n = A,T,C or G

<400> 68
ccttggtgan tctatccgna g 21

<210> 69
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<220>
<221> misc_feature

<222> 17
<223> n = A,T,C or G

<220>
<221> misc_feature
<222> 17
<223> n = A,T,C or G

<400> 69
ctgccactgc tagttgngat aatcc 25

<210> 70
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 70
gggcttctaa gcgacccaga tcttg 25

<210> 71
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 71
gaatttcctt atggacaagc tctgtgc 27

<210> 72
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 72
ggagcaggaa ctccaagacc tggag 25

<210> 73
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 73
gctcaacctc atcacatact aaccc 25

<210> 74
<211> 27
<212> DNA
<213> Artificial Sequence

<220>

<223> Primer

<400> 74
gagatgggcg ggcaagtgcg gcaacag 27

<210> 75
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 75
gcctttgcaa tcaggatcca aatttggg 28

<210> 76
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 76
ctgctgcagt tcaggaaaca tcag 24

<210> 77
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 77
accggatgtg ctcacagaac tg 22

<210> 78
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 78
tttgttatag gcatatcatt g 21

<210> 79
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 79
ttaaccagca aagtgtta 18

<210> 80

<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 80
ttagggcaag agatggtaag g 21

<210> 81
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 81
ttataacaat gatggaggg 19

<210> 82
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 82
cattaaaaag ggcacagacg c 21

<210> 83
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 83
tggacattct ccgcagt 17

<210> 84
<211> 907
<212> DNA
<213> human metapneumo virus

<400> 84
atggaggtga aagtggagaa cattcgaaca atagatatgc tcaaagcaag agtaaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcctctttgg tcctcatagg aataactaca 120
ttgagtattg ccctcaatat ctatctgatc ataaactata aaatgcaaaa aaacacatct 180
gaatcagaac atcacaccag ctcatcaccc atggaatcca gcagagaaac tccaacggtc 240
cccacagaca actcagacac caactcaagc ccacagcatc caactcaaca gtccacagaa 300
ggctccacac tctactttgc agcctcagca agctcaccag agacagaacc aacatcaaca 360
ccagatacaa caaaccgccc gcccttcgtc gacacacaca caacaccacc aagcgcaagc 420
agaacaaaga caagtccggc agtccacaca aaaaacaacc caaggacaag ctctagaaca 480
cattctccac cacgggcaac gacaaggacg gcacgcagaa ccaccactct ccgcacaagc 540
agcacaagaa agagaccgtc cacagcatca gtccaacctg acatcagcgc aacaacccac 600
aaaaacgaag aagcaagtcc agcgagccca caaacatctg caagcacaac aagaatacaa 660
aggaaaagcg tggaggccaa cacatcaaca acatacaacc aaactagtta acaaaaaata 720

caaaataact ctaagataaa ccatgcagac accaacaatg gagaagccaa aagacaattc 780
acaatctccc caaaaaggca acaacaccat attagctctg cccaaatctc cctggaaaaa 840
acactcgccc atataccaaa aataccacaa ccaccccaag aaaaaaactg ggcaaaacaa 900
cacccaa 907

<210> 85
<211> 908
<212> DNA
<213> human metapneumo virus

<400> 85
atggaggtga aagtggagaa cattcgaaca atagatatgc tcaaagcaag tgtaaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcctctttgg tcctcatagg aataactaca 120
ttgagtattg ccctcaatat ctatctgatc ataaactata aaatgcaaaa aaacacatct 180
gaatcagaac atcacaccag ctcatcaccc atggaatcca gcagagaaac tccaacggtc 240
cccacagaca actcagacac caactcaagc ccacagcatc caactcaaca gtccacagaa 300
ggctccacac tctactttgc agcctcagca agctcaccag agacagaacc aacatcaaca 360
ccagatacaa caaaccgccc gcccttcgtc gacacacaca caacaccacc aagcgcaagc 420
agaacaaaga caagtccggc agtccacaca aaaaacaacc caaggacaag ctctagaaca 480
cattctccac cacgggcaac gacaaggacg gcacgcagga accaccactc tccgcacaag 540
cagcacaaga aagagaccgt ccacagcatc agtccaacct gacatcagcg caacaaccca 600
caaaaacgaa gaagcaagtc cagcgagccc acaaacatct gcaagcacaa caagaataca 660
aaggaaaagc gtggaggcca acacatcaac aacatacaac caaactagtt aacaaaaaat 720
acaaaataac tctaagataa accatgcaga caccaacaat ggagaagcca aaagacaatt 780
cacaatctcc ccaaaaaggc aacaacacca tattagctct gcccaaatct ccctggaaaa 840
aacactcgcc catataccaa aaataccaca accaccccaa gaaaaaaact gggcaaaaca 900
acacccaa 908

<210> 86
<211> 907
<212> DNA
<213> human metapneumo virus

<400> 86
atggaggtga aagtggagaa cattcgaaca atagatatgc tcaaagcaag agtaaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcctctttgg tcctcatagg aataactaca 120
ctgagtattg ccctcaatat ctatctgatc ataaactata aaatgcaaaa aaacacatct 180
gaatcagaac atcacaccag ctcatcaccc atggaatcca gcagagaaac tccaacggtc 240
cccacagata attcagacac caactcaagc ccacaacatc caactcaaca gtccacagaa 300
ggctccacac tctactttgc agcctcagca aactcaccag agacagaacc aacatcaaca 360
ccagacacaa caaaccgccc gcccttcgtc gacacacaca caacaccacc aagcgcaagc 420
agaacaaaga caagtccggc agtccacaca aaaaacaacc caaggataag ctccagaaca 480
cactctccac catgggcaac gacaaggacg gcacgcagaa ccaccactct ccgcacaagc 540
agcacaagaa agagaccgtc cacagcatca gcccaacccg acatcagcgc aacaacccac 600
aaaaacgaag aagcaagtcc agcgagccca caaacatctg caagcacaac aagaacacaa 660
aggaaaagcg tggaggccaa cacatcaaca acatacaacc aaactagtta acaaaaaata 720
caaaataact ctaagataaa ccatgcagac accaacaatg gagaagtcaa aagacaattc 780
acaatctccc caaaaaggca acaacaccat attagctctg cccaaatctc cctggaaaaa 840
acactcgccc atataccaaa aataccacaa ccaccccaag aaaaaaactg ggcaaaacaa 900
cacccaa 907

<210> 87
<211> 907
<212> DNA
<213> human metapneumo virus

<400> 87
atggaggtga aagtggagaa cattcgaaca atagatatgc tcaaagcaag agtaaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcctctttgg tcctcatagg aataactaca 120
ttgagtattg ccctcaatat ctatctgatc ataaactata aaatgcaaaa aaacacatct 180
gaatcagaac atcacaccag ctcatcaccc atggaatcca gcagagaaac tccaacggtc 240

cccacagata attcagacac caactcaagc ccacaacatc caactcaaca gtccacagaa 300
ggctccacac tctactttgc agcctcagca aactcaccag agacagaacc aacatcaaca 360
ccagacacaa cagaccgccc gcccttcgtc gacacacaca caacaccacc aagcgcaagc 420
agaacaaaga caagtccggc agtccacaca aaaaacaacc caaggataag ctccagaaca 480
cattctccac catgggcaac gacaaggacg gcacgcagaa ccaccactct ccgcacaagc 540
agcacaagaa agagaccgtc cacagcatca gtccaacccg acatcagcgc aacaacccac 600
aaaaacgaag aagcaagtcc agcgagccca caaacatctg caagcacaac aagaacacaa 660
aggaaaagcg tggaggccaa cacatcaaca acatacaacc aaactagtta acaaaaaata 720
caaaataact ctaagataaa ccatgcagac accaacaatg gagaagtcaa aagacaattc 780
acaatctccc caaaaaggca acaacaccat attagctctg cccaaatctc cctggaaaaa 840
acactcgccc atataccaaa aataccacaa ccaccccaag aaaaaaactg ggcaaaacaa 900
cacccaa 907

<210> 88
<211> 907
<212> DNA
<213> human metapneumo virus

<400> 88
atggaggtga aagtggagaa cattcgaaca atagatatgc tcaaagcaag agtaaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcctctttgg tcctcatagg aataactaca 120
ttgagtattg ccctcaatat ctatctgatc ataaactata aaatgcaaaa aaacacatct 180
gaatcagaac atcacaccag ctcatcaccc atggaatcca gcagagaaac tccaacggtc 240
cccacagata attcagacac caactcaagc ccacaacatc caactcaaca gtccacagaa 300
ggctccacac tctactttgc agcctcagca agctcaccag agacagaacc aacatcaaca 360
ccagacacaa cagaccgccc gcccttcgtc gacacacaca caacaccacc aagcgcaagc 420
agaacaaaga caagtccggc agtccacaca aaaaacaacc caaggataag ctccagaaca 480
cattctccac catgggcaac gacaaggacg gcacgcagaa ccaccactct ccgcacaagc 540
agcacaagaa agagaccgtc cacagcatca gtccaacccg acatcagcgc aacaacccac 600
aaaaacgaag aagcaagtcc agcgagccca caaacatctg caagcacaac aagaacacaa 660
aggaaaagcg tggaggccaa cacatcaaca acatacaacc aaactagtta acaaaaaata 720
caaaataact ctaagataaa ccatgcagac accaacaatg gagaagtcaa aagacaattc 780
acaatctccc caaaaaggca acaacaccat attagctctg cccaaatctc cctggaaaaa 840
acactcgccc atataccaaa aataccacaa ccaccccaag aaaaaaactg ggcaaaacaa 900
cacccaa 907

<210> 89
<211> 907
<212> DNA
<213> human metapneumo virus

<400> 89
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cgtgtggcac gcagcaaatg ctttaaaaat gcctctttga tcctaatagg aataactaca 120
ttgagtatag ccctcaatat ctatctgatc ataaactata caatgcaaga aaacacatcc 180
gaatcagaac atcacaccag ctcatcaccc atggaatcca gcagggaaac tccaacggtc 240
cccatagaca actcagacac caatccaggc tcacagtatc caactcaaca gtccacagaa 300
gactccacac tccactctgc agcttcagca agctcaccag agacagaacc aacatcaaca 360
ccagacacaa caagccgccc gcccttcgtc gacacacaca caacaccacc aagtgcaagc 420
aggacaagga caagtccggc agtccacaca aaaaacaatc caagggtaag ccccagaaca 480
cattccccac catgggcaat gacaaggacg gtccgcggaa ccaccactct ccgcacaagc 540
agcacaagaa aaagactgtc tacagcatca gtccaacccg acagcagcgc aacaacccac 600
aaacacgaag aaacaagccc agtgagccca caaacatctg caagcacagc aagaccacaa 660
aggaagggca tggaggccag cacatcaaca acatacaacc aaactagtta acaaaaaata 720
caaaataact ctaagataaa ccatgtagac accaacaatt gagaagccaa aaggcaattc 780
acaatctccc aaaaaagcaa caacaccata ttagctccgc ttaaatctcc ctgaaaaaaa 840
cactcaccca tataccaact ataccacaac catcccaaga aaaaggctg ggcaaaacaa 900
cacccaa 907

<210> 90
<211> 908

<212> DNA
<213> human metapneumo virus

<400> 90
atggaggtga aagtggagaa cattcgaaca atagatatgc tcaaagcaag agtgaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcctctttga tcctaatagg aataactaca 120
ttgagtatag ccctcaatat ctatctgatc ataaactata caatgcaaga aaacacatcc 180
gaatcagaac atcacaccag ttcatcaccc atggaatcca gcagggaaac tccaacggtc 240
cctatggaca actcagacac caatccaggc tcacagtatc caactcaaca gtccacagaa 300
ggctccacac tccactttgc agcctcagca agctcaccag agacagaacc aacatcaaca 360
ccagacacaa caagccgccc gcccttcgtc gacacacaca caacaccatc aagtgcaagc 420
agaacaaaga caagtccggc agtccacaca aaaaacaatc taaggataag ccccagaaca 480
cattccccac catgggcaat gacaaggacg gtccgtggaa ccaccactct ccgcacaagc 540
agcataagaa aaagaccgtc cacagcatca gtccaacctg acagcagcgc aacaacccac 600
aaacacgaag aagcaagccc agtgagcccg caagcatctg caagcacagc aagaccacaa 660
aggaagggca tggaggccag cacatcaaca acatacaacc aaactagtta acaaaaaata 720
taaaataact ctaagataaa ccatgtagac accaacaatt gagaagccaa aaggcaattc 780
acaatctccc caaaaaggca acaacaccat attagctccg cttaaatctc cctggaaaaa 840
acactcgccc atataccaac tataccacaa ccatcccaag gaaaaaagct gggtaaaaca 900
acacccaa 908

<210> 91
<211> 908
<212> DNA
<213> human metapneumo virus

<400> 91
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cgtgtggcac gcagcaaatg ctttaaaaat gcctctttga tcctaatagg aataactaca 120
ttgagtatag ccctcaatat ctatctgatc ataaactata caatgcaaga aaacacatcc 180
gaatcagaac atcacaccag ctcatcaccc atggaatcca gcagagaaac tccaacggtc 240
cctatggaca actcagacac caatccaggc tcacagtatc caactcaaca gtccacagaa 300
ggctccacac tccactttgc agcctcagca agctcaccag agacagaacc aacatcaaca 360
ccagacacaa caagccgccc gcccttcgtc gacacacaca caacaccatc aagtgcaagc 420
agaataagga caagtccggc agtccacaca aaaaacaatc taaggataag ccccagaaca 480
cattccccac catgggcaat gacaaggacg gtccgtggaa ccaccactct ccgcacaagc 540
agcataagaa aaagaccgtc cacagcatca gtccaacctg acagcagcgc aacaacccac 600
aaacacgaag aagcaagccc agtgagcccg caagcatctg caagcacagc aagaccacaa 660
aggaagggca tggaggccag cacatcaaca acatacaacc aaactagtta acaaaaaata 720
tacaataact ctaagataaa ccatgtagac accaacaatt gagaagccaa aaggcaattc 780
acaatctccc caaaaaggca acaacaccat attagctccg cttaagtctc cctggaaaaa 840
acactcgccc atataccaac tataccacaa ccatccaaag aaaaaaagct gggcaaaaca 900
acacccaa 908

<210> 92
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 92
atggaggtga aagtagagaa cattcgagca atagacatgc tcaaagcaag agtgaaaaat 60
cgtgtggcac gtagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactaca 120
ctgagtatag ctctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatcc 180
gaatcagaac accacaccag ctcaccaccc acagaaccca acaaggaagc ttcaacaatc 240
tccacagaca acccagacat caatccaagc tcacagcatc caactcaaca gtccacagaa 300
aaccccacac tcaaccccgc agcatcagcg agcccatcag aaacagaacc agcatcaaca 360
ccagacacaa caaaccgcct gtcctccgta gacaggtcca cagcacaacc aagtgaaagc 420
agaacaaaga caaaaccgac agtccacaca atcaacaacc caaacacagc ttccagtaca 480
caatccccac cacggacaac aacgaaggca atccgcagag ccaccacttt ccgcatgagc 540
agcacaggaa aaagaccaac cacaacatta gtccagtccg acagcagcac cacaacccaa 600
aatcatgaag aaacaggttc agcgaaccca caggcgtctg caagcacaat gcaaaactag 660

cacaccaata atataaaacc aaattagtta acaaaaaatg cgagatagct ctaaagcaaa 720
acatgtaggt accaacaatc aagaaaccaa aagacaactc acaatctccc taaaacagca 780
acgacaccat gtcagctttg ctcaaatctc tctgggagaa acttctaccc acatactaac 840
aacatcacaa ccatctcaag aaaagaaact gggcaaaaca gcatccaa 888

<210> 93
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 93
atggaggtga aagtagagaa cattcgagca atagacatgc tcaaagcaag agtgaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactaca 120
ctgagtatag ccctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacactag ctcaccaccc acagaatcca acaaagaaac ttcaacaatc 240
cccatagaca acccagacat caatccaaac tcacagcatc caacccaaca gtccacagaa 300
agccccacac tcaaccccgc agcctcggtg agcccatcag aaacagaacc agcatcaaca 360
ccagacacaa caaaccgcct gtcctccgta gacagatcca caacacaacc aagtgaaagc 420
agaacaaaga caaaaccaac agtccacaca aaaaacaatc caagtacagt ttccagaaca 480
caatccccac tacgggcaac aacgaaggcg gtcctcagag ccaccgcttt ccgcacgagc 540
agcacaagaa aaagaccaac cacaacatca gtccagtctg acagcagcac cacaacccaa 600
aatcatgaag aaacaagttc agcgaaccca caggcatctg caagcacaat gcaaagccag 660
cacaccaaca acataaaacc aaattagtta acaaaaaata cgagatagct ctaaagtaaa 720
acatgtaggt accaacaatc aaggaatcaa aagacaactc acaatctccc taaaacagca 780
acaacatcat gtcagttttg ctcaaatctc cctgggagaa actttcgccc acatactaac 840
aacatcacaa ccatctcaag aaaagaaact gggcaaaaca gcacccaa 888

<210> 94
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 94
atggaggtga aagtagagaa catccgagca gtagacatgc tcaaagcaag agtcaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcctccttaa tcctcgtagg aataactaca 120
ctgagcatag ccctcaatat ctatctgatc gtaaactaca caatacaaaa aaccacatcc 180
gaatcagaac accacaccag ctcatcaccc acagaatcca acaaaggaac ttcaacaatc 240
cccacagaca acccagacat caatccaaat tcacaacatc caactcaaca gtccacagaa 300
agccccacac tcaacaccgc agcctcggtg agcccatcag aaacagaacc agcatcaaca 360
ccagacacaa caaaccgcct gtcctccgca gacagatcca caacacaacc aagtgaaagc 420
agaacaaaga caaagctgac agtccacaca aaaaacaacc taagtacagc ctccagaaca 480
caatcaccac cacgggcaac aacgaaggcg gtcctcagag acaccgcctt ccacacgagc 540
agcacaggaa aaagaccaac cacaacatca gtccagtctg gcagcagcac cacaactcaa 600
aatcatgaag aaacaagttc atcgaaccca caggcatctg caagcacaat gcaagaccag 660
gacaccaaca atacaaaaca aaattagtta acaaaaaata caagatagct ctaaagtaaa 720
acatgtaggt accaacagta aagaaatcaa aagacaactc acaatctccc caaaacagca 780
acaacatcat gtcagcttcg ctcaaatctc cctgggagaa actctcgccc acatactaac 840
aacatcacaa ctatctcaag aaaagaaact gggcaaaaaa acactcaa 888

<210> 95
<211> 887
<212> DNA
<213> human metapneumo virus

<400> 95
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cgtgtggcac gcagcaaatg ctttaaaaat gcctctttaa tcctcgtagg aataactaca 120
ctgagtatag ccctcaatat ctatctgatc gtaaactaca caatacaaaa aaccacatcc 180
gaatcagaac accacactag ctcatcaccc acagaatcca acaaaggaac ttcaacaatc 240
ccacagacaa cccagacatc aatccaaatt cacaacatcc aactcaacag tccacagaaa 300
gccccacact caacaccgca gcctcggtga gcccatcaga aacagaacca gcatcaacac 360

cagacacaac aaaccgcctg tcctccgcag acagatccac aacacaacca agtgaaagca 420
gaacaaagac aaagctgaca gtccacacaa aaaacaacct aagtacagcc tccagaacac 480
aatcaccacc acgggcaaca acgaaggcgg tcctcagaga caccgccttc cacacgagca 540
gcacaggaaa aagaccaacc acaacatcag tccagtctgg cagcagcacc acaactcaaa 600
atcatgaaga aacaagttca tcgaacccac aggcatctgc aagcacaatg caagaccagg 660
acaccaacaa tacaaaacaa aattagttaa caaaaaatac aagatagctc taaagtaaaa 720
catgtaggta ccaacagtaa agaaatcaaa agacaactca taatctcccc aaaacagcaa 780
caacatcatg tcagcttcgc tcaaatctcc ctgggagaaa ctctcgccca catactaaca 840
acatcacaac tatctcaaga aaagaaactg ggcaaaaaaa cactcaa 887

<210> 96
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 96
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cgtgtggcac gcagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactact 120
ctgagtatag ccctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacactag ctcaccaccc acagaatcca acaaagaaac ttcaacaatc 240
cctatagaca acccagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
agcctcacac tcaaccccgc agcctcggtg agcccatcag aaacagaacc agcatcaaca 360
ccagacacaa caaaccgcct gtcctccgta gacagatcca caacacaacc aagtgaaagc 420
agaacaaaga caaaactgac agtccacaaa aaaaacatcc caagtacagt ctctagaaca 480
caatcctcaa tacgggcaac aacgaaggcg gtcctcagag ccaccgcctt tcgcacgagc 540
agcacaggag aaagaccaac tacaacatca gtccagtctg acagcagcac cacaacccaa 600
aatcatgaag aaacaggttc agcgaaccca caggcatctg caagcacaat gcaaaactag 660
cacaccaaca ttgtaaaacc aaattagtta acaaaaaata tgaaatagct ctaaagtaaa 720
acatgtaggt gctaacaatc aagaaatcaa aagacatctc ataatctctc caaaacagca 780
acaacatcat gtcaactttg ctcaaatctc cctgggagaa actttcgccc ccatactgac 840
aacatcacaa tcatctcaag aaaagaaact gggcaaaaca gcaccaaa 888

<210> 97
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 97
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cgtgtggcac gcagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactact 120
ctgagtatag ccctcaacat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacactag ctcaccaccc acagaatcta acaaagaaac ttcaacaatc 240
tctatagaca acccagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
agcctcacac tcagccccac agcctcggtg agcccatcag aaacagaacc agcatcaaca 360
tcagacacaa caagccgcct gtcttccgta gacagatcca caacacaacc aagtgaaagc 420
agagcaagga caaaaccgac agtccacaag aaaaacatcc caagtacagt ttctagaaca 480
caatccccac tacgggcaac aacgaaggcg gtcctcagag ccaccgcctt tcgcacgagc 540
agcacaggag agggaccaac cacaacatcg gtccagtctg acagcagcac cacaacccaa 600
aatcatgaag aaacaggttc agcgaaccca caggcatctg caagcacaat gcaaaactag 660
cacaccaaca ttgtaaaacc aaattagtta acaaaaaata tgaaatagtt ctaaagtaaa 720
acatgtaggt gctaacaatc aagaaatcaa aagacaactc ataatctccc taaaacagca 780
acaacatcat gtcaactttg ctcaaatctc cctgggagaa actttcgccc ccatactgac 840
aacatcacaa tcatctcaag aaaagaaact gggcaaaaca gcaccaaa 888

<210> 98
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 98
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cgtgtggcac gtagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactaca 120
ctgagtatag ctctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacaccag ctcaccaccc acagaatcca acaaggaagc ttcaacaatc 240
tccacagaca atccagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
aaccccacac taaaccccgc agcatcggtg agctcatcag aaacagaacc agcatcaaca 360
ccagacacaa caaaccgcct gtcctccgta gacaggtcca cagcacaacc aagtgaaagc 420
agaacaaaga caaaaccgac agtccacaca agaaacaacc caagcacagc ttccagcaca 480
caatccccac cacgggtaac aacgaaggca atcctcagag ccaccgtctt ccgcatgagc 540
agcacaggaa aaagaccagc cacaacatta gtccagtccg acagcagcac cacaacccaa 600
aatcatgaag aaacaggttc agcaaactca caggcatctg caagcacaat gcaaaactag 660
cactccaaca atataaaacc aaattagtta acaaaaaata cgagatagct ctaaagtaaa 720
acatgtaggc accaacaatc aggaaattaa aagacaactc acaacctccc taaaacagca 780
acgacaccat gtcaactttg ctcaaatctc tctgggagaa acttttgccc acatactaac 840
aacatcacaa tcatctcaag aaaagaaact gggcaaaaca gcatccaa 888

<210> 99
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 99
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ctgagtatag ccctcaacat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacactag ctcaccaccc acagaatcta acaaagaaac ttcaacaatc 240
tctatagaca actcagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
agcctcacac tcagccccac agcctcggtg agcccatcag aaacagaacc agcatcaaca 360
tcagacacaa caaaccgcct gtcttccgta gacagatcca caacacaacc aagtgaaagc 420
agagcaagaa caaaaccgac agtccacaag aaaaacatcc caagtacagt ttctagaaca 480
caatccccac tacgggcaac aacgaaggcg gtcctcagag ccaccgcctt tcgcatgagc 540
agcacaggag agggaccaac cacaacatcg gtccagtctg acagcagcac cacaacccaa 600
aatcatgaag aaacaggctc agcgaaccca caggcatctg caagcacaat gcaaaaccag 660
cacaccaaca ttgcaaaacc aaattagtta acaaaaaata tgaaatagtt ctaaagtaaa 720
acatgtaggt gccaacaatc aagaaatcaa aagacaactc acaatctccc taaaacagca 780
acaacatcat gccaactttg ctcaaatctc cctgggagaa accctcgccc ccatactgac 840
aacatcacaa tcatctcaag aaaagaaact gggcaaaaca gcaccaaa 888

<210> 100
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 100
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ctgagtatag ccctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacactag ctcaccaccc acagaatcta acaaggaaac ttcaacaatc 240
cctatagaca acccagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
agcctcacac tctaccccac atcctcggtg agctcatcag aaacagaacc agcatcaaca 360
ccaggcataa caaaccacct gtcctttgta gacagatcca caacacaacc aagtgaaagc 420
agaacaaaga caaaccggac agtccacaaa aaaaacatct caagtacagt ttctagaaca 480
cagtccccac cacggacaac agcgaaggcg gtccccagag ccaccgccct tcgcacgagc 540
agcacaggag aaagaccaac cacaacacca gtccagcccg atagcagcac cacaacacaa 600
aatcatgaag aaacaggctc agcgaaccca caggcatccg caagcacaat gcaaaaccag 660
cacaccaaca ttgcaagacc aaattagtta acaaaaaata tgaaatagct ctaaagtaaa 720
acatgtaggt gccaacaatc aagaaatcaa aagataactc ataatctctc taaaacatca 780
acaacatcat gttaactttg ctcaaatctc tctgggagaa accttcgccc ccatactggc 840
aacatcacaa tcatctcaag aaaagaaact gggcaaaaca acaccaaa 888

<210> 101
<211> 888

<212> DNA
<213> human metapneumo virus

<400> 101
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cgtgtggcac gcagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactact 120
ctgagtatag ccctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacactag ctcaccaccc acagaatcta acaaggaaac ttcaacaatc 240
cctatagaca acccagacat caatccaaac tcacagcatc caactcaaca gtccgcagaa 300
agcctcacac tctaccccac atcctcggtg agctcatcag aaacagaacc agcatcaaca 360
ccaggcataa caaaccacct gtcctttgta gacagatcca caacacaacc aagtgaaagc 420
agaacaaaga caaaccggac agtccacaaa aaaaacatct caagtacagt ttctagaaca 480
cagtccccac cacggacaac agcgaaggcg gtccccagag ccaccgccct tcgcacgagc 540
agcacaggag aaagaccaac cacaacacca gtccagcccg atagcagcac cacaacacaa 600
aatcatgaag aaacaggctc agcgaaccca caggcatccg caagcacaat gcaaaaccag 660
cacaccaaca ttgcaagacc aaattagtta acaaaaaata tgaaatagct ctaaagtaaa 720
acatgtaggt gccaacaatc aagaaatcaa aagataactc ataatctctc taaaacatca 780
acaacatcat gttaactttg ctcaaatctc tctgggagaa accttcgccc ccatactggc 840
aacatcacaa tcatctcaag aaaagaaact gggcaaaaca acaccaaa 888

<210> 102
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 102
atggaggtga aagtagagaa tattcgagca atagacatgc tcaaagcaag agtgaaaaat 60
cgtgtggcac gcagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactact 120
ctgagtatag ccctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacactag ctcaccaccc acagaatcta acaaggaaac ttcaacaatc 240
cctatagaca acccagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
agcctcacac tctaccccac atcctcggtg agctcatcag aaacagaacc agcatcaaca 360
ccaggcataa caaaccacct gtcctttgta gacagatcca caacacaacc aagtgaaagc 420
agaacaaaga caaaccggac agtccacaaa aaaaacatct caagtacagt ttctagaaca 480
cagtccccac cacggacaac agcgaaggcg gtccccagag ccaccgccct tcgcacgagc 540
agcacaggag aaagaccaac cacaacacca gtccagcccg atagcagcac cacaacacaa 600
aatcatgaag aaacaggctc agcgaaccca caggcatccg caagcacaat gcaaaaccag 660
cacaccaaca ttgcaagacc aaattagtta acaaaaaata tgaaatagct ctaaagtaaa 720
acatgtaggt gccaacaatc aagaaatcaa aagataactc ataatctctc taaaacatca 780
acaacatcat gttaactttg ctcaaatctc tctgggagaa accttcgccc ccatactggc 840
aacatcacaa tcatctcaag aaaagaaact gggcaaaaca acacccaa 888

<210> 103
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 103
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cgtgtggcac gtagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactaca 120
ctgagcatag ccctcaatat ctatctgatc ataaactaca caatacaaca aaccacatct 180
gaatcagaac accacaccag ctcaccaccc acagaatcca acaaggaagc ttcaacaatc 240
tccacagaca acccagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
aaccccacac tcaacccagc agcatcagcg agcccatcag aaacagaatc agcatcaaca 360
ccagatacaa caaaccgcct gtcctccgta gacaggtcca cggtacaacc aagtgaaaac 420
agaacaaaga caaaactgac agtccacaca agaaacaacc taagcacagc ctccagtaca 480
caatccccac cacgggcaac aacgaaggca atccgcagag ccaccaccct ccgcatgagc 540
agcacaggaa gaagaccaac cacaacacta gtccagtccg acagcagcac cacaacccaa 600
aatcatgaag aaacaggctc agcgaaccca caggcatctg caagcacaat gcaaaaccag 660
cacaccaaca atataaaacc aaattagtta acaaaaaata cgagatagct ctaaagtaaa 720
acatgtaggc accaacaatc aagaaaccaa aagataactc acaatccccc caaaacagca 780

acgacaccat gtcagctttg ctcaaatctc tctgggagaa acttttgccc acatactaac 840
aacatcacaa ccatctcaag aaaagaaact gggcaaaaca gcatccaa 888

<210> 104
<211> 888
<212> DNA
<213> human metapneumo virus

<400> 104
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cgtgtggcac gtagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactaca 120
ctgagcatag ccctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatct 180
gaatcagaac accacaccag ctcaccaccc acagaatcca acaaggaagc ttcaacaatc 240
tccacagaca acccagacat caatccaaac tcacagcatc caactcaaca gtccacagaa 300
aaccccacac tcaacccagc agcatcagcg agcccatcag aaacagaatc agcatcaaca 360
ccagatacaa caaaccgcct gtcctccgta gacaggtcca cggtacaacc aagtgaaaac 420
agaacaaaga caaaactgac agtccacaca agaaacaacc taagcacagc ctccagtaca 480
caatccccac cacgggcaac aacgaaggca atccgcagag ccaccaccct ccgcatgagc 540
agcacaggaa gaagaccaac cacaacacta gtccagtccg acagcagcac cacaacccaa 600
aatcatgaag aaacaggctc agcgaaccca caggcatctg caagcacaat gcaaaaccag 660
cacaccaaca atataaaacc aaattagtta acaaaaaata cgagatagct ctaaagtaaa 720
acatgtaggc accaacaatc aagaaaccaa aagataactc acaatccccc caaaacagca 780
acgacaccat gtcagctttg ctcaaatctc tctgggagaa acttttgccc acatactaac 840
aacatcacaa ccatctcaag aaaagaaact gggcaaaaca gcatccaa 888

<210> 105
<211> 901
<212> DNA
<213> human metapneumo virus

<400> 105
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cgtataagaa gcagcaggtg ctatagaaat gctacactga tccttattgg actaacagcg 120
ttaagcatgg cacttaatat tttcctgatc atcgatcatg caacattaag aaacatgatc 180
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tccacagcag gcccaaacac caaacccaat ccacagcaag caacacagtg gaccacagag 300
aactcaacat ccccagtagc aaccccagag ggccatccat acacagggac aactcaaaca 360
tcagacacaa cagctcccca gcaaaccaca gacaaacaca cagcaccgct aaaatcaacc 420
aatgaacaga tcacccagac aaccacagag aaaaagacaa tcagagcaac aacccaaaaa 480
agggaaaaag gaaaagaaaa cacaaaccaa accacaagca cagctgcaac ccaaacaacc 540
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ccacaccatg catagagagg tgcaaaactc aaatgagcac aacacacaaa catcccatcc 720
aagtagttaa caaaaaacca caaaataacc ttgaaaacca aaaaaccaaa acataaaccc 780
agacccagaa aaacatagac accatatgga aggttctagc atatgcacca atgagatggc 840
atctgttcat gtatcaatag caccaccatc attcaaggaa taagaagagg cgaaaattta 900
a 901

<210> 106
<211> 901
<212> DNA
<213> human metapneumo virus

<400> 106
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cgtataagaa gcagcaggtg ctatagaaat gctacactga tccttattgg actaacagcg 120
ttaagcatgg cacttaatat tttcctgatc attgatcatg caacattaag aaacatgatc 180
aaaacagaaa actgtgctaa catgccatcg gcagaaccaa gcaaaaagac cccaatgacc 240
tccacagcag gcccaagcac cgaacccaat ccacagcaag caacacaatg gaccacagag 300
aactcaacat ccccagcagc aaccctagag agccatccat acacagggac aacccaaaca 360
ccagacataa cagctcccca acaaaccaca gacaaacaca cagcactgcc aaaatcaacc 420

aatgaacaga tcacccagac aaccacagag aaaaagacaa ccagagcaac aacccaaaaa 480
agggaaaaag aaaaagaaaa cacaaaccaa accacaagca cagctgcaac ccaaacaacc 540
aacaccacca accaaaccag aaatgcaagt gagacaatca caacatccga cagacccaga 600
attgacacca caacccaaag cagcgatcag acaacccggg caacagaccc aagctcccca 660
ccacaccatg cacagagtgg tgcaaaaccc aaatgaacac aacacacaaa catctcatcc 720
aagtagttaa caaaaaacca caaaataacc ttgaaaacca aaaaaccaaa ccacaaactt 780
agacccagaa aacatagac actatatgga aggtttgagc atatgcacca atgaaatggt 840
atctgttcat gtatcaatag cgccaccatt atttaaggaa taagaagagg caaaaattca 900
a 901

<210> 107
<211> 860
<212> DNA
<213> human metapneumo virus

<400> 107
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ttaagcatgg cacttaatat tttcctgatc atcgatcatg caacattaag aaacatgatc 180
aaaacagaaa attgtgctaa catgccgccg gcagaaccaa gcaaaaagac cccaatgacc 240
tctacagcag gcccaaacac caaacccaat ccacagcaag caacacagtg gaccacggag 300
aactcaacat tcccagcagc aacctcagag ggccatctac acacagggac aactcaaaca 360
ccagacacaa cagctcctca gcaaaccaca gacaaacaca cagcactgcc aaaatcaacc 420
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ccacatcatg cacagggaag tgcaaaaccc aaatgaacac aacacacaaa catcccatcc 720
aagtagttaa caaaaaatca gacccagaaa aacatagaca ctatatggaa ggtccgagca 780
tatgcaccga tgaaatggca tttgttcatg tatcaatagc gccaccatta tttaaggaat 840
aagaagaggc aaaaattcaa 860

<210> 108
<211> 861
<212> DNA
<213> human metapneumo virus

<400> 108
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cgtataagaa gcagcaggtg ctatagaaat gctacactga tccttattgg actaacagcg 120
ttaagcatgg cacttaatat tttcctgatc atcgatcatg caacattaag aaacatgatc 180
aaaacagaaa attgtgctaa catgccgccg gcagaaccaa gcagaaagac cccaatgacc 240
tccacagcag gcccaaacac caaacccaat ccacagcaag caacacagtg gaccacggag 300
aactcaacat ccccagcagc aaccccagag ggccatctac acacagggac aactcaaaca 360
ccagacacaa cagctcctca gcaaaccaca gacaaacaca cagcactgcc aaaatcaacc 420
aatgaacaga tcacccaggc aaccacagag aaaaagacaa ccagagaaac aacccaaaga 480
agggaaaaag gaaaagaaaa cacaaaccaa accacaagca cagctgcaac ccaaacaacc 540
aacaccacca accaaatcag aaatgcaagc gagacaatca caacatccga cagacccaga 600
actgactcca caacccaaag cagcgaacag acaacccagg caacagaccc aagctcccca 660
gcacaccatg cacagggaag tgcaaaaccc aaatgaacac aacacacaaa catcccatcc 720
aagtagttaa caaaaaaatc agacccagaa aaacacagac actatatgga aggtccgagc 780
atatgcaccg atgaaatggc atctgttcat gtatcaatag caccaccatt atttaaggaa 840
taagaagagg caaaaattca a 861

<210> 109
<211> 860
<212> DNA
<213> human metapneumo virus

<400> 109
atggaagtaa gagtggagaa cattcgagcg atagacatgt tcaaagcaaa gataaaaaac 60

cgtataagaa gcagcaggtg ctatagaaat gctacattga tccttattgg actaacagcg 120
ttaagcatgg cacttaatat tttcctgatc atcgatcatg caacattaag aaacatgatc 180
aaaacagaaa attgtgctaa catgccaccg gcagaaccaa gcaaaaagac cccaatgacc 240
tccacagcag gcctaaacac taaacccaat ccacagcaag caacacagtg gaccacggag 300
aactcaacat ccccagcagc aaccccagag ggccatctac acacagggac aactcaaaca 360
ccagacacaa cagctcctca gcaaaccaca gacaagcaca cagcactgcc aaaatcaacc 420
aatgaacaga tcacccagac aaccacagag aaaaagacaa ccagagcaac aacccaaaga 480
agggaaaaag gaaaagaaaa cacaaaccaa accacaagca cagctgcaac ccaaacaacc 540
aacaccacca accaaatcag aaatgcaagc gagacaatca caacatccga cagacccaga 600
actgactcca caacccaaag cagcgaacag acaacccggg caacagaccc aagctcccca 660
ccacaccatg cacagggaag tgcaaaaccc aaatgaacac aacacacaaa catcccatcc 720
aagtagttaa caaaaaatca gacccagaaa aacatagaca ctatatggaa ggtccgagca 780
tatgcaccga tgaaatggca tctgttcatg tatcaatagc gccaccatta tttaaggaat 840
aagaagaggc aaaaattcaa 860

<210> 110
<211> 860
<212> DNA
<213> human metapneumo virus

<400> 110
atggaagtaa gagtggagaa cattcgagcg atagacatgt tcaaagcaaa gataaaaaac 60
cgtataagaa gcagcaggtg ctatagaaat gctacactga tccttattgg actaacagcg 120
ttaagcatgg cacttaatat tttcctgatc atcgatcatg caacattaag aaacatgatc 180
aaaacagaaa attgtgctaa catgccgccg gcagaaccaa gcaaaaagac cccaatgacc 240
tccacagcag gcccaaacac caaacccaat ccacagcaag caacacagtg gaccacggag 300
aactcaacat ccccagcagc aaccccagag ggccatctac acacagggac aactcaaaca 360
ccagacacaa cagctcctca gcaaaccaca gacaaacaca cagcactgcc aaaatcaacc 420
aatgaacaga tcacccagac aaccacagag aaaaagacaa ccagagcaac aacccaaaga 480
agggaaaaag gaaaagaaaa cacaaaccaa accacaagca cagctgcaac ccaaacaacc 540
aacaccacca accaaatcag aaatgcaatt gagacaatca caacatccga cagacccaga 600
actgactcca caacccaaag cagcgaacag acaacccggg caacagaccc aagctcccac 660
ccacaccatg cacagggaag tgcaaaaccc aaatgaacac aacacacaaa catcccatcc 720
aagtagttaa caaaaaatca gacccagaaa aacatagaca ctatatggaa ggtccgagca 780
tatgcaccga tgaaatggca tctgttcatg tatcaatagc gccaccatta tttaaggaat 840
aagaagaggc aagaattcaa 860

<210> 111
<211> 886
<212> DNA
<213> human metapneumo virus

<400> 111
atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa aatgaaaaac 60
cgtataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attaacagca 120
ttaagtatgg cacttaatat ttttttaatc attgattatg caatgttaaa aaacatgacc 180
aaagtggaac actgtgttaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag acttaaacac caaacccaat ccacagcagg caacacagtt ggccgcagag 300
gattcaacat ctctagcagc aacctcagag gaccatctac acacagggac aactccaaca 360
ccagatgcaa cagtctctca gcaaaccaca gacgagtaca caacattgct gagatcaacc 420
aacagacaga ccacccaaac aaccacagag aaaaagccaa ccggagcaac aaccaaaaaa 480
gaaaccacaa ctcgaactac aagcacagct gcaacccaaa cactcaacac taccaaccaa 540
actagctatg tgagagaggc aaccacaaca tccgccagat ccagaaacag tgccacaact 600
caaagcagcg accaaacaac ccaggcagca gacccaagct cccaaccaca ccatacacag 660
aaaagcacaa caacaacata caacacagac acatcctctc caagtagtta acaaaaaaac 720
tataaaataa tcatgaaaac cgaaaaacta gaaaagttaa tttgaactca gaaagaaca 780
caaacactat atgaattgtt tgagcgtata tactaatgaa atagcatctg tttgtgcatc 840
aataatacca tcattattta agaaataaga agaagctaaa attcaa 886

<210> 112
<211> 889

<212> DNA
<213> human metapneumo virus

<400> 112
atggaagtaa gagtggagaa cattcggaca atagacatgt tcaaagcaaa gatgaaaaac 60
cgtataagaa gcagcaagtg ctatagaaat gctacactga tccttattgg actgacagca 120
ttaagtatgg cacttaatat tttcttgatc atcgattatg caacatttaa aaacatgacc 180
aaagtggaac actgtgctaa tatgccgccg gtagaaccga gtaagaagac cccaatgacc 240
tctacagtag actcaagcac cggacccaat ccacagcaga caacacagtg gaccacagag 300
gattcaacat ctctagcagc aacctcagag gaccatctac acacagggac aactccaaca 360
ctagatgcaa cagtttctca gcaaacccca gacaagcaca caacaccgct gagatcaacc 420
aatggacaga ccacccagac aaccacagag aaaaagccaa ccagagcaat agccaaaaaa 480
gaaaccacaa accaaaccac aagcacagct gcaacccaaa cattcaacac caccaatcaa 540
accagaaatg gaagagagac aaccataaca tctgccagat ccagaaacga cgccacaact 600
caaagcagcg aacaaacaaa ccagacaaca gacccaagct cccaaccaca tcatgcatag 660
ataagcacaa taacaatatg aacacaacac agacacatct tctccaagta gttaacaaaa 720
aactataaaa taaccatgaa aaccaaaaaa ctagaaaagt aaatttgaac tcagaaaaga 780
acacaaacac taaatgaatt gtttgagcat atatactaat gaaatagcat ctgttcatgc 840
atcaataata ccatcattac ttaagaaata agaagaagca aaaattcaa 889

<210> 113
<211> 885
<212> DNA
<213> human metapneumo virus

<400> 113
atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa gatgaaaaac 60
cgtataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attaacagca 120
ttaagtatgg cacttaatat ttttttaatc attgattatg caatgttaaa aaacatgacc 180
aaagtggaac actgtgttaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag acttaaacac caaactcaat ccacagcagg caacacagtt gaccacagag 300
gattcaacat ctctagcagc aacctcggag gatcatttac tcacagggac aactccaaca 360
ccagatgcaa cagtctctca gcaaaccaca gacgagcaca caacactgct gagatcaacc 420
aacagacaga ccacccaaac aaccacagag aaaaagccaa ccggagcaac aaccaaaaaa 480
gaaaccacaa ctcgaaccac aagcacagct gcaacccaaa cactcaacac caccaaccaa 540
actagcaatg gaagagaggc aaccacaaca tccaccagat ccagaaacgg tgccacaact 600
caaaacagcg atcaaacaac ctagacagca gacccaagct cccaaccaca ccatacacag 660
aaaagcacaa caacaacata caacacagac acatcttctc caagtagtta acaaaaaact 720
ataaaataac catgaaaact aaaaaactag aaaagttaat ttgaactcag aaaagaacac 780
aaacactata tgaattgttt gagcgtatat actaatgaaa tagcatctgt ttgtgcatca 840
ataataccat cattatttaa gaaataagaa gaagctaaaa ttcaa 885

<210> 114
<211> 885
<212> DNA
<213> human metapneumo virus

<400> 114
atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa gatgaaaaac 60
cgcataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attaacagca 120
ttaagtatgg cacttaatat ttttttaatc attgattatg caacattaaa aaacatgacc 180
aaagtggaac actgtgttaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag acttaaacac caaactcaat ccacagcagg caacacagtt gaccacagag 300
gattcaacat ctctagcagc aacctcagag ggccatccac acacaggaac aactccaaca 360
ccagacgcaa cagtctctca gcaaaccaca gacgagcaca caacactgct gagatcaacc 420
aacagacaga ccacccaaac agccacagag aaaaagccaa ctggagcaac aaccaaaaaa 480
gaaaccacaa cccgaactac aagtacagct gcaacccaaa cacccaacac caccaaccaa 540
accagcaatg gaagagaggc aaccacaaca tccgccaggt ccagaaacgg tgccacaact 600
caaaacagcg atcaaataac ccaggcagca gactcaagct cccaaccaca ccatacacag 660
aaaagcacaa caacagcata caacacagac acatcttttc caagtagtta acaaaaaact 720
ataaaataac catgaaaacc aaaaaactag aaaagttaat ttgaactcag aaaagaacac 780

aaacactata tgaattgttt gagcgtatat actaatgaaa tagcatctgt ttgtgcatca 840
ataataccat cattatttaa gaaataagaa gaagctaaaa ttcaa 885

<210> 115
<211> 886
<212> DNA
<213> human metapneumo virus

<400> 115
atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa gatgaaaaac 60
cgtataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attaacagca 120
ctaagtatgg cacttaatat ttttttaatc attgattatg caacattaaa aaacatgacc 180
aaagtggaac actgtgttaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag actcaaacac caaacccaat ccacagcagg caacacagtt gaccacagag 300
gattctacat ctttagcagc aaccctagag gaccatccac acacagggac aactccaaca 360
ccagatgcaa cagtctctca gcaaaccaca gacgagcaca caacactgct gagatcaacc 420
aacagacaga ccacccaaac aactgcagag aaaaagccaa ccagggcaac aaccaaaaaa 480
gaaaccacaa ctcgaaccac aagcacagct gcaacccaaa cactcaacac caccaaccaa 540
actagcaatg gaagagaggc aaccacaaca tctgccagat ccagaaacaa tgccacaact 600
caaagcagcg atcaaacaac ccaggcagca gaaccaagct cccaatcaca acatacacag 660
aaaagcacaa caacaacata caacacagac acatcttctc taagtagtta acaaaaaaac 720
tataaaataa ccatgaaaac caaaaaacta gaaaagttaa tttgaactca gaaaagaaca 780
caaacactat atgaattatt tgagcgtata tactaatgaa atagcatctg tttgtgcatc 840
aataatacca tcattattta agaaataaga agaagctaaa attcaa 886

<210> 116
<211> 887
<212> DNA
<213> human metapneumo virus

<400> 116
atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa gatgaaaaac 60
cgtataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attatcagca 120
ctaagtatgg cacttaatat ttttttaatc attgattatg caaaatcaaa aaacatgacc 180
agagtggaac actgtgtcaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag acttaaacac caaacccaat ccacagcggg caacacagtt gaccacagag 300
gattcaacat ctctagcagc aaccctagag ggccatctac acacagggac aactccaaca 360
ccagatgtaa cagtctctca gcaaaccaca gacgagcaca caacactgct gagatcaacc 420
aacagacaga ccacccaaac agccgcagag aaaaagccaa ccagagtaac aactaacaaa 480
gaaaccataa ctcgaaccac aagcacagcc gcaacccaaa cactcaacac caccaaccaa 540
accaacaatg gaagagaggc aaccacaaca tctgccagat ccagaaacaa tgccacaact 600
caaagcagcg accaaacaac ccaggcagca gacccaagct cccaatcaca acatacacag 660
aaaagcataa caacaacata caacacagac acatcttctc caagtagtta acaaaaaaac 720
tataaaataa ccatgaaaac caaaaaaact agaaaagtta atttgaactc agaaaagaac 780
acaaacacta tatgaattgt ttgagcgtat atactaatga aatagcatct gtttgtgcat 840
caataatacc atcattattt aagaattaag aagaagctaa aattcaa 887

<210> 117
<211> 887
<212> DNA
<213> human metapneumo virus

<400> 117
atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa gatgaaaaac 60
cgtataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attatcagca 120
ctaagtatgg cacttaatat ttttttaatc attgattatg caaaatcaaa aaccatgacc 180
agagtggaac actgtgttaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag acttaaacac caaacccaat ccacagcagg caacacagtt gaccacagag 300
gattcaacat ctccagcagc aaccctagag ggccatctac acacagggac aactccaaca 360
ccagatgcaa cagtctctca gcaaaccaca gacgagcaca caacactgct gagatcaacc 420
aacagacaga ccacccaaac aaccgcagag aaaaagccaa ccagagcaac aaccaaaaaa 480

```
gaaaccataa ctcgaaccac aagcacagct gcaacccaaa cactcaacac caccaaccaa 540
accagcaatg gaagagaggc aaccacaaca tctgccagat ccagaaacaa tgccacaact 600
caaagcagcg accaaacaac ccaggcagca gacccaagct cccaatcaca acatacaaag 660
aaaagcacaa caacaacata caacacagac acatcttctc caagtagtta acaaaaaaac 720
tataaaataa ccatgaaaac caaaaaaact agaaaagtta atttgaactc agaaaagaac 780
acaaacacta tatgaattgt ttgagcgtat atactaatga aatagcatct gtttgtgcat 840
caataatacc atcattattt aagaattaag aagaagctaa aattcaa               887
```

<210> 118
<211> 886
<212> DNA
<213> human metapneumo virus

<400> 118

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atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa gatgaaaaac 60
cgtataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attaacagca 120
ctaagtatgg cacttaatat ttttttaatc attgattatg caacattaaa aaacatgacc 180
aaagtggaac actgtgttaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag acttaaacac caaacccaat ccacagcagg caacacagtt gaccacagag 300
gactctacat ctttagcagc aaccctagag gaccatccac acacagggac aactccaaca 360
ccagatgcaa cagtctctca gcaaaccaca gacgagcaca caacactgct gagatcaacc 420
aacagacaga ccacccaaac aactgcagag aaaaagccaa ccagagcaac aaccaaaaaa 480
gaaaccacaa ctcgaaccac aagcacagct gcaacccaaa cactcaacac caccaaccaa 540
actagcaatg gaagagaggc aaccacaaca tctgccagat ccagaaacaa tgccacaact 600
caaagcagcg atcaaacaac ccaagcagca gaaccaaact cccaatcaca acatacacag 660
aaaagcacaa caacaacata caacacagac acatcttctc taagtagtta acaaaaaaac 720
tataaaataa ccatgaaaac caaaaaacta gaaaagttaa tttgaactca gaaaggaaca 780
caaacactat atgaattatt tgagcgtata tactaatgaa atagcatctg tttgtgcatc 840
aataatacca tcattattta agaaataaga agaagctaaa attcaa                886
```

<210> 119
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 119

```
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1               5                   10                  15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20                  25                  30
Leu Val Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35                  40                  45
Leu Ile Ile Asn Tyr Lys Met Gln Lys Asn Thr Ser Glu Ser Glu His
    50                  55                  60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65                  70                  75                  80
Pro Thr Asp Asn Ser Asp Thr Asn Ser Ser Pro Gln His Pro Thr Gln
                85                  90                  95
Gln Ser Thr Glu Gly Ser Thr Leu Tyr Phe Ala Ala Ser Ala Ser Ser
            100                 105                 110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Asn Arg Pro Pro
        115                 120                 125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Lys Thr
    130                 135                 140
Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Thr Ser Ser Arg Thr
145                 150                 155                 160
His Ser Pro Pro Arg Ala Thr Thr Arg Thr Ala Arg Arg Thr Thr Thr
                165                 170                 175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
            180                 185                 190
Pro Asp Ile Ser Ala Thr Thr His Lys Asn Glu Glu Ala Ser Pro Ala
```

```
        195                     200                     205
Ser Pro Gln Thr Ser Ala Ser Thr Thr Arg Ile Gln Arg Lys Ser Val
    210                     215                     220
Glu Ala Asn Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225                     230                     235
```

<210> 120
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 120

```
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
 1               5                  10                  15
Ser Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20                  25                  30
Leu Val Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35                  40                  45
Leu Ile Ile Asn Tyr Lys Met Gln Lys Asn Thr Ser Glu Ser Glu His
    50                  55                  60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65                  70                  75                  80
Pro Thr Asp Asn Ser Asp Thr Asn Ser Ser Pro Gln His Pro Thr Gln
                85                  90                  95
Gln Ser Thr Glu Gly Ser Thr Leu Tyr Phe Ala Ala Ser Ala Ser Ser
            100                 105                 110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Asn Arg Pro Pro
        115                 120                 125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Lys Thr
    130                 135                 140
Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Thr Ser Ser Arg Thr
145                 150                 155                 160
His Ser Pro Pro Arg Ala Thr Thr Arg Thr Ala Arg Arg Thr Thr Thr
                165                 170                 175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
            180                 185                 190
Pro Asp Ile Ser Ala Thr Thr His Lys Asn Glu Glu Ala Ser Pro Ala
        195                 200                 205
Ser Pro Gln Thr Ser Ala Ser Thr Thr Arg Ile Gln Arg Lys Ser Val
    210                 215                 220
Glu Ala Asn Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225                 230                 235
```

<210> 121
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 121

```
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
 1               5                  10                  15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20                  25                  30
Leu Val Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35                  40                  45
Leu Ile Ile Asn Tyr Lys Met Gln Lys Asn Thr Ser Glu Ser Glu His
    50                  55                  60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65                  70                  75                  80
```

Pro Thr Asp Asn Ser Asp Thr Asn Ser Ser Pro Gln His Pro Thr Gln
                85   90   95
Gln Ser Thr Glu Gly Ser Thr Leu Tyr Phe Ala Ala Ser Ala Asn Ser
            100   105   110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Asn Arg Pro Pro
        115   120   125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Lys Thr
    130   135   140
Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Ile Ser Ser Arg Thr
145   150   155   160
His Ser Pro Pro Trp Ala Thr Thr Arg Thr Ala Arg Arg Thr Thr Thr
                165   170   175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Pro Ser Thr Ala Ser Ala Gln
            180   185   190
Pro Asp Ile Ser Ala Thr Thr His Lys Asn Glu Glu Ala Ser Pro Ala
        195   200   205
Ser Pro Gln Thr Ser Ala Ser Thr Thr Arg Thr Gln Arg Lys Ser Val
    210   215   220
Glu Ala Asn Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225   230   235

<210> 122
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 122
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1   5   10   15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20   25   30
Leu Val Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35   40   45
Leu Ile Ile Asn Tyr Lys Met Gln Lys Asn Thr Ser Glu Ser Glu His
    50   55   60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65   70   75   80
Pro Thr Asp Asn Ser Asp Thr Asn Ser Ser Pro Gln His Pro Thr Gln
                85   90   95
Gln Ser Thr Glu Gly Ser Thr Leu Tyr Phe Ala Ala Ser Ala Asn Ser
            100   105   110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Asp Arg Pro Pro
        115   120   125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Lys Thr
    130   135   140
Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Ile Ser Ser Arg Thr
145   150   155   160
His Ser Pro Pro Trp Ala Thr Thr Arg Thr Ala Arg Arg Thr Thr Thr
                165   170   175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
            180   185   190
Pro Asp Ile Ser Ala Thr Thr His Lys Asn Glu Glu Ala Ser Pro Ala
        195   200   205
Ser Pro Gln Thr Ser Ala Ser Thr Thr Arg Thr Gln Arg Lys Ser Val
    210   215   220
Glu Ala Asn Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225   230   235

<210> 123

<211> 236
<212> PRT
<213> human metapneumo virus

<400> 123
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Val Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Lys Met Gln Lys Asn Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65 70 75 80
Pro Thr Asp Asn Ser Asp Thr Asn Ser Ser Pro Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Gly Ser Thr Leu Tyr Phe Ala Ala Ser Ala Ser Ser
100 105 110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Asp Arg Pro Pro
115 120 125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Lys Thr
130 135 140
Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Ile Ser Ser Arg Thr
145 150 155 160
His Ser Pro Pro Trp Ala Thr Thr Arg Thr Ala Arg Arg Thr Thr Thr
165 170 175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
180 185 190
Pro Asp Ile Ser Ala Thr Thr His Lys Asn Glu Glu Ala Ser Pro Ala
195 200 205
Ser Pro Gln Thr Ser Ala Ser Thr Thr Arg Thr Gln Arg Lys Ser Val
210 215 220
Glu Ala Asn Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225 230 235

<210> 124
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 124
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Met Gln Glu Asn Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65 70 75 80
Pro Ile Asp Asn Ser Asp Thr Asn Pro Gly Ser Gln Tyr Pro Thr Gln
85 90 95
Gln Ser Thr Glu Asp Ser Thr Leu His Ser Ala Ala Ser Ala Ser Ser
100 105 110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Ser Arg Pro Pro
115 120 125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Arg Thr
130 135 140

Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Val Ser Pro Arg Thr
145 150 155 160
His Ser Pro Pro Trp Ala Met Thr Arg Thr Val Arg Gly Thr Thr Thr
165 170 175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Leu Ser Thr Ala Ser Val Gln
180 185 190
Pro Asp Ser Ser Ala Thr Thr His Lys His Glu Glu Thr Ser Pro Val
195 200 205
Ser Pro Gln Thr Ser Ala Ser Thr Ala Arg Pro Gln Arg Lys Gly Met
210 215 220
Glu Ala Ser Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225 230 235

<210> 125
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 125
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Met Gln Glu Asn Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65 70 75 80
Pro Met Asp Asn Ser Asp Thr Asn Pro Gly Ser Gln Tyr Pro Thr Gln
85 90 95
Gln Ser Thr Glu Gly Ser Thr Leu His Phe Ala Ala Ser Ala Ser Ser
100 105 110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Ser Arg Pro Pro
115 120 125
Phe Val Asp Thr His Thr Thr Pro Ser Ser Ala Ser Arg Thr Lys Thr
130 135 140
Ser Pro Ala Val His Thr Lys Asn Asn Leu Arg Ile Ser Pro Arg Thr
145 150 155 160
His Ser Pro Pro Trp Ala Met Thr Arg Thr Val Arg Gly Thr Thr Thr
165 170 175
Leu Arg Thr Ser Ser Ile Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
180 185 190
Pro Asp Ser Ser Ala Thr Thr His Lys His Glu Glu Ala Ser Pro Val
195 200 205
Ser Pro Gln Ala Ser Ala Ser Thr Ala Arg Pro Gln Arg Lys Gly Met
210 215 220
Glu Ala Ser Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225 230 235

<210> 126
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 126
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser

```
            20                      25                      30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35                      40                      45
Leu Ile Ile Asn Tyr Thr Met Gln Glu Asn Thr Ser Glu Ser Glu His
    50                      55                      60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65                      70                      75                      80
Pro Met Asp Asn Ser Asp Thr Asn Pro Gly Ser Gln Tyr Pro Thr Gln
                85                      90                      95
Gln Ser Thr Glu Gly Ser Thr Leu His Phe Ala Ala Ser Ala Ser Ser
            100                     105                     110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Ser Arg Pro Pro
        115                     120                     125
Phe Val Asp Thr His Thr Thr Pro Ser Ser Ala Ser Arg Ile Arg Thr
    130                     135                     140
Ser Pro Ala Val His Thr Lys Asn Asn Leu Arg Ile Ser Pro Arg Thr
145                     150                     155                     160
His Ser Pro Pro Trp Ala Met Thr Arg Thr Val Arg Gly Thr Thr Thr
                165                     170                     175
Leu Arg Thr Ser Ser Ile Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
            180                     185                     190
Pro Asp Ser Ser Ala Thr Thr His Lys His Glu Glu Ala Ser Pro Val
        195                     200                     205
Ser Pro Gln Ala Ser Ala Ser Thr Ala Arg Pro Gln Arg Lys Gly Met
    210                     215                     220
Glu Ala Ser Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225                     230                     235


<210> 127
<211> 228
<212> PRT
<213> Human metapneumo virus

<220>
<221> VARIANT
<222> 220
<223> Xaa = unknown amino acid or other

<400> 127
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
 1               5                  10                  15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20                  25                  30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35                  40                  45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
    50                  55                  60
His Thr Ser Ser Pro Pro Thr Glu Pro Asn Lys Glu Ala Ser Thr Ile
65                  70                  75                  80
Ser Thr Asp Asn Pro Asp Ile Asn Pro Ser Ser Gln His Pro Thr Gln
                85                  90                  95
Gln Ser Thr Glu Asn Pro Thr Leu Asn Pro Ala Ala Ser Ala Ser Pro
            100                 105                 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
        115                 120                 125
Ser Val Asp Arg Ser Thr Ala Gln Pro Ser Glu Ser Arg Thr Lys Thr
    130                 135                 140
Lys Pro Thr Val His Thr Ile Asn Asn Pro Asn Thr Ala Ser Ser Thr
145                 150                 155                 160
Gln Ser Pro Pro Arg Thr Thr Thr Lys Ala Ile Arg Arg Ala Thr Thr
```

165 170 175
Phe Arg Met Ser Ser Thr Gly Lys Arg Pro Thr Thr Thr Leu Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Xaa His Thr Asn Asn
210 215 220
Ile Lys Pro Asn
225

<210> 128
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 128
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Thr Ser Thr Ile
65 70 75 80
Pro Ile Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Ser Pro Thr Leu Asn Pro Ala Ala Ser Val Ser Pro
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Thr Lys Thr
130 135 140
Lys Pro Thr Val His Thr Lys Asn Asn Pro Ser Thr Val Ser Arg Thr
145 150 155 160
Gln Ser Pro Leu Arg Ala Thr Thr Lys Ala Val Leu Arg Ala Thr Ala
165 170 175
Phe Arg Thr Ser Ser Thr Arg Lys Arg Pro Thr Thr Thr Ser Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Ser Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Ser Gln His Thr Asn Asn
210 215 220
Ile Lys Pro Asn
225

<210> 129
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 129
Met Glu Val Lys Val Glu Asn Ile Arg Ala Val Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Val Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45

Leu Ile Val Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Ser Pro Thr Glu Ser Asn Lys Gly Thr Ser Thr Ile
65 70 75 80
Pro Thr Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Ser Pro Thr Leu Asn Thr Ala Ala Ser Val Ser Pro
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Ala Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Thr Lys Thr
130 135 140
Lys Leu Thr Val His Thr Lys Asn Asn Leu Ser Thr Ala Ser Arg Thr
145 150 155 160
Gln Ser Pro Pro Arg Ala Thr Thr Lys Ala Val Leu Arg Asp Thr Ala
165 170 175
Phe His Thr Ser Ser Thr Gly Lys Arg Pro Thr Thr Thr Ser Val Gln
180 185 190
Ser Gly Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Ser Ser Ser
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asp Gln Asp Thr Asn Asn
210 215 220
Thr Lys Gln Asn
225

<210> 130
<211> 228
<212> PRT
<213> human metapneumo virus

<220>
<221> VARIANT
<222> 81
<223> Xaa = Any Amino Acid

<400> 130
Met Glu Val Lys Val Glu Asn Ile Arg Ala Val Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Val Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Val Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Ser Pro Thr Glu Ser Asn Lys Gly Thr Ser Thr Ile
65 70 75 80
Xaa Thr Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Ser Pro Thr Leu Asn Thr Ala Ala Ser Val Ser Pro
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Ala Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Thr Lys Thr
130 135 140
Lys Leu Thr Val His Thr Lys Asn Asn Leu Ser Thr Ala Ser Arg Thr
145 150 155 160
Gln Ser Pro Pro Arg Ala Thr Thr Lys Ala Val Leu Arg Asp Thr Ala
165 170 175
Phe His Thr Ser Ser Thr Gly Lys Arg Pro Thr Thr Thr Ser Val Gln
180 185 190

Ser Gly Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Ser Ser Ser
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asp Gln Asp Thr Asn Asn
210 215 220
Thr Lys Gln Asn
225

<210> 131
<211> 228
<212> PRT
<213> Human metapneumo virus

<220>
<221> VARIANT
<222> 220
<223> Xaa = unknown amino acid or other

<400> 131
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Met Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Thr Ser Thr Ile
65 70 75 80
Pro Ile Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Ser Leu Thr Leu Asn Pro Ala Ala Ser Val Ser Pro
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Thr Lys Thr
130 135 140
Lys Leu Thr Val His Lys Lys Asn Ile Pro Ser Thr Val Ser Arg Thr
145 150 155 160
Gln Ser Ser Ile Arg Ala Thr Thr Lys Ala Val Leu Arg Ala Thr Ala
165 170 175
Phe Arg Thr Ser Ser Thr Gly Glu Arg Pro Thr Thr Thr Ser Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Xaa His Thr Asn Ile
210 215 220
Val Lys Pro Asn
225

<210> 132
<211> 228
<212> PRT
<213> Human metapneumovirus

<220>
<221> VARIANT
<222> 220
<223> Xaa = unknown amino acid or other

<400> 132
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Thr Ser Thr Ile
65 70 75 80
Ser Ile Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Ser Leu Thr Leu Ser Pro Thr Ala Ser Val Ser Pro
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Ser Asp Thr Thr Ser Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Ala Arg Thr
130 135 140
Lys Pro Thr Val His Lys Lys Asn Ile Pro Ser Thr Val Ser Arg Thr
145 150 155 160
Gln Ser Pro Leu Arg Ala Thr Thr Lys Ala Val Leu Arg Ala Thr Ala
165 170 175
Phe Arg Thr Ser Ser Thr Gly Glu Gly Pro Thr Thr Thr Ser Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Xaa His Thr Asn Ile
210 215 220
Val Lys Pro Asn
225

<210> 133
<211> 228
<212> PRT
<213> Human metapneumovirus

<220>
<221> VARIANT
<222> 220
<223> Xaa = unknown amino acid or other

<400> 133
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Ala Ser Thr Ile
65 70 75 80
Ser Thr Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Asn Pro Thr Leu Asn Pro Ala Ala Ser Val Ser Ser
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Ala Gln Pro Ser Glu Ser Arg Thr Lys Thr

130 135 140
Lys Pro Thr Val His Thr Arg Asn Asn Pro Ser Thr Ala Ser Ser Thr
145 150 155 160
Gln Ser Pro Pro Arg Val Thr Thr Lys Ala Ile Leu Arg Ala Thr Val
165 170 175
Phe Arg Met Ser Ser Thr Gly Lys Arg Pro Ala Thr Thr Leu Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Ser Gln Ala Ser Ala Ser Thr Met Gln Asn Xaa His Ser Asn Asn
210 215 220
Ile Lys Pro Asn
225

<210> 134
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 134
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Thr Ser Thr Ile
65 70 75 80
Ser Ile Asp Asn Ser Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Ser Leu Thr Leu Ser Pro Thr Ala Ser Val Ser Pro
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Ser Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Ala Arg Thr
130 135 140
Lys Pro Thr Val His Lys Lys Asn Ile Pro Ser Thr Val Ser Arg Thr
145 150 155 160
Gln Ser Pro Leu Arg Ala Thr Thr Lys Ala Val Leu Arg Ala Thr Ala
165 170 175
Phe Arg Met Ser Ser Thr Gly Glu Gly Pro Thr Thr Thr Ser Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Gln His Thr Asn Ile
210 215 220
Ala Lys Pro Asn
225

<210> 135
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 135
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15

Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Thr Ser Thr Ile
65 70 75 80
Pro Ile Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Ser Leu Thr Leu Tyr Pro Thr Ser Ser Val Ser Ser
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Gly Ile Thr Asn His Leu Ser
115 120 125
Phe Val Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Thr Lys Thr
130 135 140
Asn Arg Thr Val His Lys Lys Asn Ile Ser Ser Thr Val Ser Arg Thr
145 150 155 160
Gln Ser Pro Pro Arg Thr Thr Ala Lys Ala Val Pro Arg Ala Thr Ala
165 170 175
Leu Arg Thr Ser Ser Thr Gly Glu Arg Pro Thr Thr Thr Pro Val Gln
180 185 190
Pro Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Gln His Thr Asn Ile
210 215 220
Ala Arg Pro Asn
225

<210> 136
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 136
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Thr Ser Thr Ile
65 70 75 80
Pro Ile Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Ala Glu Ser Leu Thr Leu Tyr Pro Thr Ser Ser Val Ser Ser
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Gly Ile Thr Asn His Leu Ser
115 120 125
Phe Val Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Thr Lys Thr
130 135 140
Asn Arg Thr Val His Lys Lys Asn Ile Ser Ser Thr Val Ser Arg Thr
145 150 155 160
Gln Ser Pro Pro Arg Thr Thr Ala Lys Ala Val Pro Arg Ala Thr Ala
165 170 175
Leu Arg Thr Ser Ser Thr Gly Glu Arg Pro Thr Thr Thr Pro Val Gln
180 185 190
Pro Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala

```
        195                 200                 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Gln His Thr Asn Ile
    210                 215                 220
Ala Arg Pro Asn
225


<210> 137
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 137
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1               5                   10                  15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20                  25                  30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35                  40                  45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
    50                  55                  60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Thr Ser Thr Ile
65                  70                  75                  80
Pro Ile Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
                85                  90                  95
Gln Ser Thr Glu Ser Leu Thr Leu Tyr Pro Thr Ser Ser Val Ser Ser
            100                 105                 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Gly Ile Thr Asn His Leu Ser
        115                 120                 125
Phe Val Asp Arg Ser Thr Thr Gln Pro Ser Glu Ser Arg Thr Lys Thr
    130                 135                 140
Asn Arg Thr Val His Lys Lys Asn Ile Ser Ser Thr Val Ser Arg Thr
145                 150                 155                 160
Gln Ser Pro Pro Arg Thr Thr Ala Lys Ala Val Pro Arg Ala Thr Ala
                165                 170                 175
Leu Arg Thr Ser Ser Thr Gly Glu Arg Pro Thr Thr Thr Pro Val Gln
            180                 185                 190
Pro Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
        195                 200                 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Gln His Thr Asn Ile
    210                 215                 220
Ala Arg Pro Asn
225


<210> 138
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 138
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1               5                   10                  15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20                  25                  30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35                  40                  45
Leu Ile Ile Asn Tyr Thr Ile Gln Gln Thr Thr Ser Glu Ser Glu His
    50                  55                  60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Ala Ser Thr Ile
65                  70                  75                  80
```

Ser Thr Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Asn Pro Thr Leu Asn Pro Ala Ala Ser Ala Ser Pro
100 105 110
Ser Glu Thr Glu Ser Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Val Gln Pro Ser Glu Asn Arg Thr Lys Thr
130 135 140
Lys Leu Thr Val His Thr Arg Asn Asn Leu Ser Thr Ala Ser Ser Thr
145 150 155 160
Gln Ser Pro Pro Arg Ala Thr Thr Lys Ala Ile Arg Arg Ala Thr Thr
165 170 175
Leu Arg Met Ser Ser Thr Gly Arg Arg Pro Thr Thr Thr Leu Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Gln His Thr Asn Asn
210 215 220
Ile Lys Pro Asn
225

<210> 139
<211> 228
<212> PRT
<213> human metapneumo virus

<400> 139
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Ser Asn Lys Glu Ala Ser Thr Ile
65 70 75 80
Ser Thr Asp Asn Pro Asp Ile Asn Pro Asn Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Asn Pro Thr Leu Asn Pro Ala Ala Ser Ala Ser Pro
100 105 110
Ser Glu Thr Glu Ser Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Val Gln Pro Ser Glu Asn Arg Thr Lys Thr
130 135 140
Lys Leu Thr Val His Thr Arg Asn Asn Leu Ser Thr Ala Ser Ser Thr
145 150 155 160
Gln Ser Pro Pro Arg Ala Thr Thr Lys Ala Ile Arg Arg Ala Thr Thr
165 170 175
Leu Arg Met Ser Ser Thr Gly Arg Arg Pro Thr Thr Thr Leu Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn Gln His Thr Asn Asn
210 215 220
Ile Lys Pro Asn
225

<210> 140

<211> 231
<212> PRT
<213> Human metapneumo virus

<220>
<221> VARIANT
<222> 225
<223> Xaa = unknown amino acid or other

<400> 140
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Ile Lys Asn Arg Ile Arg Ser Ser Arg Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp His Ala Thr Leu Arg Asn Met Ile Lys Thr Glu Asn
50 55 60
Cys Ala Asn Met Pro Ser Ala Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Thr Ala Gly Pro Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
85 90 95
Trp Thr Thr Glu Asn Ser Thr Ser Pro Val Ala Thr Pro Glu Gly His
100 105 110
Pro Tyr Thr Gly Thr Thr Gln Thr Ser Asp Thr Thr Ala Pro Gln Gln
115 120 125
Thr Thr Asp Lys His Thr Ala Pro Leu Lys Ser Thr Asn Glu Gln Ile
130 135 140
Thr Gln Thr Thr Thr Glu Lys Lys Thr Ile Arg Ala Thr Thr Gln Lys
145 150 155 160
Arg Glu Lys Gly Lys Glu Asn Thr Asn Gln Thr Thr Ser Thr Ala Ala
165 170 175
Thr Gln Thr Thr Asn Thr Thr Asn Gln Ile Arg Asn Ala Ser Glu Thr
180 185 190
Ile Thr Thr Ser Asp Arg Pro Arg Thr Asp Thr Thr Thr Gln Ser Ser
195 200 205
Glu Gln Thr Thr Arg Ala Thr Asp Pro Ser Ser Pro Pro His His Ala
210 215 220
Xaa Arg Gly Ala Lys Leu Lys
225 230

<210> 141
<211> 231
<212> PRT
<213> human metapneumo virus

<400> 141
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Ile Lys Asn Arg Ile Arg Ser Ser Arg Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp His Ala Thr Leu Arg Asn Met Ile Lys Thr Glu Asn
50 55 60
Cys Ala Asn Met Pro Ser Ala Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Thr Ala Gly Pro Ser Thr Glu Pro Asn Pro Gln Gln Ala Thr Gln
85 90 95
Trp Thr Thr Glu Asn Ser Thr Ser Pro Ala Ala Thr Leu Glu Ser His

```
            100                     105                     110
Pro Tyr Thr Gly Thr Thr Gln Thr Pro Asp Ile Thr Ala Pro Gln Gln
        115                     120                     125
Thr Thr Asp Lys His Thr Ala Leu Pro Lys Ser Thr Asn Glu Gln Ile
    130                     135                     140
Thr Gln Thr Thr Thr Glu Lys Lys Thr Thr Arg Ala Thr Thr Gln Lys
145                     150                     155                 160
Arg Glu Lys Glu Lys Glu Asn Thr Asn Gln Thr Thr Ser Thr Ala Ala
                165                     170                     175
Thr Gln Thr Thr Asn Thr Thr Asn Gln Thr Arg Asn Ala Ser Glu Thr
            180                     185                     190
Ile Thr Thr Ser Asp Arg Pro Arg Ile Asp Thr Thr Thr Gln Ser Ser
        195                     200                     205
Asp Gln Thr Thr Arg Ala Thr Asp Pro Ser Ser Pro Pro His His Ala
    210                     215                     220
Gln Ser Gly Ala Lys Pro Lys
225                     230
```

<210> 142
<211> 231
<212> PRT
<213> human metapneumo virus

<400> 142

```
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1               5                   10                  15
Lys Ile Lys Asn Arg Ile Arg Ser Ser Arg Cys Tyr Arg Asn Ala Thr
            20                  25                  30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
        35                  40                  45
Leu Ile Ile Asp His Ala Thr Leu Arg Asn Met Ile Lys Thr Glu Asn
    50                  55                  60
Cys Ala Asn Met Pro Pro Ala Glu Pro Ser Lys Lys Thr Pro Met Thr
65                  70                  75                  80
Ser Thr Ala Gly Pro Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
                85                  90                  95
Trp Thr Thr Glu Asn Ser Thr Phe Pro Ala Ala Thr Ser Glu Gly His
            100                 105                 110
Leu His Thr Gly Thr Thr Gln Thr Pro Asp Thr Thr Ala Pro Gln Gln
        115                 120                 125
Thr Thr Asp Lys His Thr Ala Leu Pro Lys Ser Thr Asn Glu Gln Ile
    130                 135                 140
Thr Gln Thr Thr Thr Glu Lys Lys Thr Thr Arg Ala Thr Thr Gln Arg
145                 150                 155                 160
Arg Glu Lys Gly Lys Glu Asn Thr Asn Gln Thr Thr Ser Thr Ala Ala
                165                 170                 175
Thr Gln Thr Thr Asn Thr Thr Asn Gln Ile Arg Asn Ala Ser Glu Thr
            180                 185                 190
Ile Thr Thr Ser Asp Arg Pro Arg Thr Asp Ser Thr Thr Gln Ser Ser
        195                 200                 205
Glu Gln Thr Thr Arg Ala Thr Asp Pro Ser Ser Pro Pro His His Ala
    210                 215                 220
Gln Gly Ser Ala Lys Pro Lys
225                 230
```

<210> 143
<211> 231
<212> PRT
<213> human metapneumo virus

<400> 143
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Ile Lys Asn Arg Ile Arg Ser Ser Arg Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp His Ala Thr Leu Arg Asn Met Ile Lys Thr Glu Asn
50 55 60
Cys Ala Asn Met Pro Pro Ala Glu Pro Ser Arg Lys Thr Pro Met Thr
65 70 75 80
Ser Thr Ala Gly Pro Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
85 90 95
Trp Thr Thr Glu Asn Ser Thr Ser Pro Ala Ala Thr Pro Glu Gly His
100 105 110
Leu His Thr Gly Thr Thr Gln Thr Pro Asp Thr Thr Ala Pro Gln Gln
115 120 125
Thr Thr Asp Lys His Thr Ala Leu Pro Lys Ser Thr Asn Glu Gln Ile
130 135 140
Thr Gln Ala Thr Thr Glu Lys Lys Thr Thr Arg Glu Thr Thr Gln Arg
145 150 155 160
Arg Glu Lys Gly Lys Glu Asn Thr Asn Gln Thr Thr Ser Thr Ala Ala
165 170 175
Thr Gln Thr Thr Asn Thr Thr Asn Gln Ile Arg Asn Ala Ser Glu Thr
180 185 190
Ile Thr Thr Ser Asp Arg Pro Arg Thr Asp Ser Thr Thr Gln Ser Ser
195 200 205
Glu Gln Thr Thr Gln Ala Thr Asp Pro Ser Ser Pro Ala His His Ala
210 215 220
Gln Gly Ser Ala Lys Pro Lys
225 230

<210> 144
<211> 231
<212> PRT
<213> human metapneumo virus

<400> 144
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Ile Lys Asn Arg Ile Arg Ser Ser Arg Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp His Ala Thr Leu Arg Asn Met Ile Lys Thr Glu Asn
50 55 60
Cys Ala Asn Met Pro Pro Ala Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Thr Ala Gly Leu Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
85 90 95
Trp Thr Thr Glu Asn Ser Thr Ser Pro Ala Ala Thr Pro Glu Gly His
100 105 110
Leu His Thr Gly Thr Thr Gln Thr Pro Asp Thr Thr Ala Pro Gln Gln
115 120 125
Thr Thr Asp Lys His Thr Ala Leu Pro Lys Ser Thr Asn Glu Gln Ile
130 135 140
Thr Gln Thr Thr Thr Glu Lys Lys Thr Thr Arg Ala Thr Thr Gln Arg
145 150 155 160
Arg Glu Lys Gly Lys Glu Asn Thr Asn Gln Thr Thr Ser Thr Ala Ala

```
                165                     170                     175
Thr Gln Thr Thr Asn Thr Thr Asn Gln Ile Arg Asn Ala Ser Glu Thr
            180                     185                     190
Ile Thr Thr Ser Asp Arg Pro Arg Thr Asp Ser Thr Thr Gln Ser Ser
        195                     200                     205
Glu Gln Thr Thr Arg Ala Thr Asp Pro Ser Ser Pro Pro His His Ala
    210                     215                     220
Gln Gly Ser Ala Lys Pro Lys
225                     230
```

<210> 145
<211> 231
<212> PRT
<213> human metapneumo virus

<400> 145

```
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1               5                   10                  15
Lys Ile Lys Asn Arg Ile Arg Ser Ser Arg Cys Tyr Arg Asn Ala Thr
            20                  25                  30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
        35                  40                  45
Leu Ile Ile Asp His Ala Thr Leu Arg Asn Met Ile Lys Thr Glu Asn
    50                  55                  60
Cys Ala Asn Met Pro Pro Ala Glu Pro Ser Lys Lys Thr Pro Met Thr
65                  70                  75                  80
Ser Thr Ala Gly Pro Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
                85                  90                  95
Trp Thr Thr Glu Asn Ser Thr Ser Pro Ala Ala Thr Pro Glu Gly His
            100                 105                 110
Leu His Thr Gly Thr Thr Gln Thr Pro Asp Thr Thr Ala Pro Gln Gln
        115                 120                 125
Thr Thr Asp Lys His Thr Ala Leu Pro Lys Ser Thr Asn Glu Gln Ile
    130                 135                 140
Thr Gln Thr Thr Thr Glu Lys Lys Thr Thr Arg Ala Thr Thr Gln Arg
145                 150                 155                 160
Arg Glu Lys Gly Lys Glu Asn Thr Asn Gln Thr Thr Ser Thr Ala Ala
                165                 170                 175
Thr Gln Thr Thr Asn Thr Thr Asn Gln Ile Arg Asn Ala Ile Glu Thr
            180                 185                 190
Ile Thr Thr Ser Asp Arg Pro Arg Thr Asp Ser Thr Thr Gln Ser Ser
        195                 200                 205
Glu Gln Thr Thr Arg Ala Thr Asp Pro Ser Ser His Pro His His Ala
    210                 215                 220
Gln Gly Ser Ala Lys Pro Lys
225                 230
```

<210> 146
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 146

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Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1               5                   10                  15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
            20                  25                  30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
        35                  40                  45
```

Leu Ile Ile Asp Tyr Ala Met Leu Lys Asn Met Thr Lys Val Glu His
50 55 60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Ala Val Asp Leu Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
85 90 95
Leu Ala Ala Glu Asp Ser Thr Ser Leu Ala Ala Thr Ser Glu Asp His
100 105 110
Leu His Thr Gly Thr Thr Pro Thr Pro Asp Ala Thr Val Ser Gln Gln
115 120 125
Thr Thr Asp Glu Tyr Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
130 135 140
Thr Gln Thr Thr Thr Glu Lys Lys Pro Thr Gly Ala Thr Thr Lys Lys
145 150 155 160
Glu Thr Thr Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Leu Asn
165 170 175
Thr Thr Asn Gln Thr Ser Tyr Val Arg Glu Ala Thr Thr Thr Ser Ala
180 185 190
Arg Ser Arg Asn Ser Ala Thr Thr Gln Ser Ser Asp Gln Thr Thr Gln
195 200 205
Ala Ala Asp Pro Ser Ser Gln Pro His His Thr Gln Lys Ser Thr Thr
210 215 220
Thr Thr Tyr Asn Thr Asp Thr Ser Ser Pro Ser Ser
225 230 235

<210> 147
<211> 236
<212> PRT
<213> Human metapneumo virus

<220>
<221> VARIANT
<222> 220, 227
<223> Xaa = unknown amino acid or other

<400> 147
Met Glu Val Arg Val Glu Asn Ile Arg Thr Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp Tyr Ala Thr Phe Lys Asn Met Thr Lys Val Glu His
50 55 60
Cys Ala Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Thr Val Asp Ser Ser Thr Gly Pro Asn Pro Gln Gln Thr Thr Gln
85 90 95
Trp Thr Thr Glu Asp Ser Thr Ser Leu Ala Ala Thr Ser Glu Asp His
100 105 110
Leu His Thr Gly Thr Thr Pro Thr Leu Asp Ala Thr Val Ser Gln Gln
115 120 125
Thr Pro Asp Lys His Thr Thr Pro Leu Arg Ser Thr Asn Gly Gln Thr
130 135 140
Thr Gln Thr Thr Thr Glu Lys Lys Pro Thr Arg Ala Ile Ala Lys Lys
145 150 155 160
Glu Thr Thr Asn Gln Thr Thr Ser Thr Ala Ala Thr Gln Thr Phe Asn
165 170 175
Thr Thr Asn Gln Thr Arg Asn Gly Arg Glu Thr Thr Ile Thr Ser Ala
180 185 190

Arg Ser Arg Asn Asp Ala Thr Thr Gln Ser Ser Glu Gln Thr Asn Gln
195 200 205
Thr Thr Asp Pro Ser Ser Gln Pro His His Ala Xaa Ile Ser Thr Ile
210 215 220
Thr Ile Xaa Thr Gln His Arg His Ile Phe Ser Lys
225 230 235

<210> 148
<211> 236
<212> PRT
<213> Human metapneumo virus

<220>
<221> VARIANT
<222> 208
<223> Xaa = unknown amino acid or other

<400> 148
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp Tyr Ala Met Leu Lys Asn Met Thr Lys Val Glu His
50 55 60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Ala Val Asp Leu Asn Thr Lys Leu Asn Pro Gln Gln Ala Thr Gln
85 90 95
Leu Thr Thr Glu Asp Ser Thr Ser Leu Ala Ala Thr Ser Glu Asp His
100 105 110
Leu Leu Thr Gly Thr Thr Pro Thr Pro Asp Ala Thr Val Ser Gln Gln
115 120 125
Thr Thr Asp Glu His Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
130 135 140
Thr Gln Thr Thr Thr Glu Lys Lys Pro Thr Gly Ala Thr Thr Lys Lys
145 150 155 160
Glu Thr Thr Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Leu Asn
165 170 175
Thr Thr Asn Gln Thr Ser Asn Gly Arg Glu Ala Thr Thr Thr Ser Thr
180 185 190
Arg Ser Arg Asn Gly Ala Thr Thr Gln Asn Ser Asp Gln Thr Thr Xaa
195 200 205
Thr Ala Asp Pro Ser Ser Gln Pro His His Thr Gln Lys Ser Thr Thr
210 215 220
Thr Thr Tyr Asn Thr Asp Thr Ser Ser Pro Ser Ser
225 230 235

<210> 149
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 149
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe

```
        35                      40                      45
Leu Ile Ile Asp Tyr Ala Thr Leu Lys Asn Met Thr Lys Val Glu His
    50                      55                      60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65                      70                      75                      80
Ser Ala Val Asp Leu Asn Thr Lys Leu Asn Pro Gln Gln Ala Thr Gln
                85                      90                      95
Leu Thr Thr Glu Asp Ser Thr Ser Leu Ala Ala Thr Ser Glu Gly His
            100                     105                     110
Pro His Thr Gly Thr Thr Pro Thr Pro Asp Ala Thr Val Ser Gln Gln
        115                     120                     125
Thr Thr Asp Glu His Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
    130                     135                     140
Thr Gln Thr Ala Thr Glu Lys Lys Pro Thr Gly Ala Thr Thr Lys Lys
145                     150                     155                     160
Glu Thr Thr Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Pro Asn
                165                     170                     175
Thr Thr Asn Gln Thr Ser Asn Gly Arg Glu Ala Thr Thr Thr Ser Ala
            180                     185                     190
Arg Ser Arg Asn Gly Ala Thr Thr Gln Asn Ser Asp Gln Ile Thr Gln
        195                     200                     205
Ala Ala Asp Ser Ser Ser Gln Pro His His Thr Gln Lys Ser Thr Thr
    210                     215                     220
Thr Ala Tyr Asn Thr Asp Thr Ser Phe Pro Ser Ser
225                     230                     235
```

<210> 150
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 150

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Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1               5                   10                  15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
            20                  25                  30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
        35                  40                  45
Leu Ile Ile Asp Tyr Ala Thr Leu Lys Asn Met Thr Lys Val Glu His
    50                  55                  60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65                  70                  75                  80
Ser Ala Val Asp Ser Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
                85                  90                  95
Leu Thr Thr Glu Asp Ser Thr Ser Leu Ala Ala Thr Leu Glu Asp His
            100                 105                 110
Pro His Thr Gly Thr Thr Pro Thr Pro Asp Ala Thr Val Ser Gln Gln
        115                 120                 125
Thr Thr Asp Glu His Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
    130                 135                 140
Thr Gln Thr Thr Ala Glu Lys Lys Pro Thr Arg Ala Thr Thr Lys Lys
145                 150                 155                 160
Glu Thr Thr Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Leu Asn
                165                 170                 175
Thr Thr Asn Gln Thr Ser Asn Gly Arg Glu Ala Thr Thr Thr Ser Ala
            180                 185                 190
Arg Ser Arg Asn Asn Ala Thr Thr Gln Ser Ser Asp Gln Thr Thr Gln
        195                 200                 205
Ala Ala Glu Pro Ser Ser Gln Ser Gln His Thr Gln Lys Ser Thr Thr
    210                 215                 220
```

Thr Thr Tyr Asn Thr Asp Thr Ser Ser Leu Ser Ser
225 230 235

<210> 151
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 151
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Ser Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp Tyr Ala Lys Ser Lys Asn Met Thr Arg Val Glu His
50 55 60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Ala Val Asp Leu Asn Thr Lys Pro Asn Pro Gln Arg Ala Thr Gln
85 90 95
Leu Thr Thr Glu Asp Ser Thr Ser Leu Ala Ala Thr Leu Glu Gly His
100 105 110
Leu His Thr Gly Thr Thr Pro Thr Pro Asp Val Thr Val Ser Gln Gln
115 120 125
Thr Thr Asp Glu His Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
130 135 140
Thr Gln Thr Ala Ala Glu Lys Lys Pro Thr Arg Val Thr Thr Asn Lys
145 150 155 160
Glu Thr Ile Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Leu Asn
165 170 175
Thr Thr Asn Gln Thr Asn Asn Gly Arg Glu Ala Thr Thr Thr Ser Ala
180 185 190
Arg Ser Arg Asn Asn Ala Thr Thr Gln Ser Ser Asp Gln Thr Thr Gln
195 200 205
Ala Ala Asp Pro Ser Ser Gln Ser Gln His Thr Gln Lys Ser Ile Thr
210 215 220
Thr Thr Tyr Asn Thr Asp Thr Ser Ser Pro Ser Ser
225 230 235

<210> 152
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 152
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Ser Ala Leu Ser Met Ala Leu Asn Ile Phe
35 40 45
Leu Ile Ile Asp Tyr Ala Lys Ser Lys Thr Met Thr Arg Val Glu His
50 55 60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65 70 75 80
Ser Ala Val Asp Leu Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
85 90 95
Leu Thr Thr Glu Asp Ser Thr Ser Pro Ala Ala Thr Leu Glu Gly His

```
            100                     105                     110
Leu His Thr Gly Thr Thr Pro Thr Pro Asp Ala Thr Val Ser Gln Gln
        115                     120                     125
Thr Thr Asp Glu His Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
    130                     135                     140
Thr Gln Thr Thr Ala Glu Lys Lys Pro Thr Arg Ala Thr Thr Lys Lys
145                     150                     155                 160
Glu Thr Ile Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Leu Asn
                165                     170                     175
Thr Thr Asn Gln Thr Ser Asn Gly Arg Glu Ala Thr Thr Thr Ser Ala
            180                     185                     190
Arg Ser Arg Asn Asn Ala Thr Thr Gln Ser Ser Asp Gln Thr Thr Gln
        195                     200                     205
Ala Ala Asp Pro Ser Ser Gln Ser Gln His Thr Lys Lys Ser Thr Thr
    210                     215                     220
Thr Thr Tyr Asn Thr Asp Thr Ser Ser Pro Ser Ser
225                     230                     235


<210> 153
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 153
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1               5                   10                  15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
            20                  25                  30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
        35                  40                  45
Leu Ile Ile Asp Tyr Ala Thr Leu Lys Asn Met Thr Lys Val Glu His
    50                  55                  60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65                  70                  75                  80
Ser Ala Val Asp Leu Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
                85                  90                  95
Leu Thr Thr Glu Asp Ser Thr Ser Leu Ala Ala Thr Leu Glu Asp His
            100                 105                 110
Pro His Thr Gly Thr Thr Pro Thr Pro Asp Ala Thr Val Ser Gln Gln
        115                 120                 125
Thr Thr Asp Glu His Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
    130                 135                 140
Thr Gln Thr Thr Ala Glu Lys Lys Pro Thr Arg Ala Thr Thr Lys Lys
145                 150                 155                 160
Glu Thr Thr Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Leu Asn
                165                 170                 175
Thr Thr Asn Gln Thr Ser Asn Gly Arg Glu Ala Thr Thr Thr Ser Ala
            180                 185                 190
Arg Ser Arg Asn Asn Ala Thr Thr Gln Ser Ser Asp Gln Thr Thr Gln
        195                 200                 205
Ala Ala Glu Pro Asn Ser Gln Ser Gln His Thr Gln Lys Ser Thr Thr
    210                 215                 220
Thr Thr Tyr Asn Thr Asp Thr Ser Ser Leu Ser Ser
225                 230                 235


<210> 154
<211> 449
<212> DNA
<213> human metapneumo virus
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<400> 154
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgtt caggaaaaaa gggaaactat 120
gcttgcctct taagagaaga ccaaggatgg tattgtcaaa atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg tgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacataa acatatctac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactatc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 155
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 155
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgct cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga tcaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacatca acatatccac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 156
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 156
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgct cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga tcaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagattg cgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacatca acatatccac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 157
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 157
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgct cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga tcaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacatca acatatccac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 158
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 158
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgct cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga tcaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagattg cgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacatca acatatccac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gtagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 159
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 159
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgtt cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga ccaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg tgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacataa acatatctac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 160
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 160
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgtt cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga ccaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg tgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacataa acatatctac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 161
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 161
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgtt cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga ccaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg tgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacataa acatatctac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 162
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 162

ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggggttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgct cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga tcagggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg tgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacatca acatatccac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtaggaatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 163
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 163
ataggagttt acggaagctc cgtaatttac atggtgcaac tgccaatctt tggagttata 60
gacacgcctt gctggatagt aaaagcagcc ccttcttgct cagaaaaaaa gggaaactat 120
gcttgcctct taagagaaga tcaaggatgg tattgtcaga atgcagggtc aactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggagaccatg tcttttgcga cacagcagca 240
ggaatcaatg ttgctgagca gtcaaaggag tgcaacatca acatatccac tactaattac 300
ccatgcaaag ttagcacagg aagacatcct atcagtatgg ttgcactgtc tcctcttggg 360
gctttggttg cttgctacaa gggagtgagc tgttccattg gcagcaacag agtagggatc 420
atcaagcaac tgaacaaagg ctgctctta 449

<210> 164
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 164
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<213> human metapneumo virus

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<210> 214
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<212> DNA
<213> human metapneumo virus

<400> 214
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<210> 216
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 216
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<210> 217
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<213> human metapneumo virus

<400> 217
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ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa gggggttagc tgctcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 218
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 218
atagggtct acggaagctc tgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac caccaactac 300
ccatgcaaag tcagcacagg aagacacccc atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgctcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 219
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 219
atagggggtct acggaagctc tgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac caccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgctcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 220
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 220
atagggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga ccaagggtgg tattgtaaaa atgcgggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 221
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 221
atagggggtct acggaagctc cgtgatttac atggtccagc taccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagctgca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatccac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactgtc acctctcggc 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 222
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 222
atagggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac taccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 223
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 223

atagggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg tgaaacaaga ggtgatcatg tttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 224
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 224
atagggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga ccaagggtgg tattgtaaaa atgcgggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg tttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 225
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 225
atagggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg tttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 226
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 226
atagggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg tgaaacaaga ggtgatcatg tttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 227
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 227
atagggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60

gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg tttttgtga cacagctgca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcaattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 228
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 228
ataggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg tttttgtga cacagctgca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcaattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 229
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 229
ataggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg tttttgtga cacagctgca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa ggggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 230
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 230
ataggggtct acggaagctc tgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg tttttgtga cacagctgca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatccac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactgtc acctctcggc 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 231
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 231
ataggggtct acggaagctc tgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120

gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagcagca 240
gggatcaacg ttgctgagca atcaagagaa tgcaacatca acatatctac caccaactat 300
ccgtgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgctcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 232
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 232
ataggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagctgca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcaattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 233
<211> 449
<212> DNA
<213> human metapneumo virus

<400> 233
ataggggtct acggaagctc cgtgatttac atggtccagc tgccgatctt tggtgtcata 60
gatacacctt gttggataat caaggcagct ccctcttgtt cagaaaaaga tggaaattat 120
gcttgcctcc taagagagga tcaagggtgg tattgtaaaa atgcaggatc cactgtttac 180
tacccaaatg aaaaagactg cgaaacaaga ggtgatcatg ttttttgtga cacagcagca 240
gggatcaatg ttgctgagca atcaagagaa tgcaacatca acatatctac aaccaactac 300
ccatgcaaag tcagcacagg aagacaccct atcagcatgg ttgcactatc acctctcggt 360
gctttggtag cttgctacaa aggggttagc tgttcgattg gcagtaatcg ggttggaata 420
atcaaacaac tacctaaagg ctgctcata 449

<210> 234
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 234
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1   5   10   15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20   25   30
Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35   40   45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50   55   60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65   70   75   80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85   90   95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100   105   110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115   120   125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130   135   140

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Asn Lys Gly Cys Ser
145


<210> 235
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 235
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 236
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 236
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 237
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<211> 149
<212> PRT
<213> human metapneumo virus

<400> 237
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Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145
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<210> 238
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 238
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Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145
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<210> 239
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 239

Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 240
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 240
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 241
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 241
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln

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        35                      40                      45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                      60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                      80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                      95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 242
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 242
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                      15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                      30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                      80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                      95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 243
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 243
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                      15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                      30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                      80
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Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 244
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 244
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 245
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 245
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly

```
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145
```

<210> 246
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 246

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145
```

<210> 247
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 247

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Arg Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145
```

<210> 248
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 248
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 249
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 249
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 250
<211> 149
<212> PRT

<213> human metapneumo virus

<400> 250
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 251
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 251
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 252
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 252
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15

Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 253
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 253
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 254
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 254
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu

50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 255
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 255
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 256
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 256
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95

Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 257
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 257
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 258
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 258
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu

130 135 140
Asn Lys Gly Cys Ser
145

<210> 259
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 259
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 260
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 260
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 261
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 261
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 262
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 262
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 263
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 263
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 264
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 264
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 265
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 265
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30

```
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Val Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 266
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 266
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 267
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 267
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
```

```
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145
```

```
<210> 268
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 268
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1              5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145
```

```
<210> 269
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 269
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1              5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
```

Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125

Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140

Asn Lys Gly Cys Ser
145

<210> 270
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 270
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15

Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30

Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45

Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60

Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80

Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95

Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110

Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125

Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140

Asn Lys Gly Cys Ser
145

<210> 271
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 271
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15

Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30

Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45

Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60

Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80

Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95

Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110

Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125

Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140

Asn Lys Gly Cys Ser

145

<210> 272
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 272
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 273
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 273
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 274
<211> 149

<212> PRT
<213> human metapneumo virus

<400> 274
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 275
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 275
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Asn Lys Gly Cys Ser
145

<210> 276
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 276
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile

```
 1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 277
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 277
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Asn Lys Gly Cys Ser
145


<210> 278
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 278
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
```

Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 279
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 279
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Trp Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 280
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 280
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser

```
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 281
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 281

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 282
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 282

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1               5                   10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
```

Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 283
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 283
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 284
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 284
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 285
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 285
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Ser Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 286
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 286
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 287
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 287
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 288
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 288
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 289
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 289
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser

```
            20                      25                      30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                      45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                      60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                      80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                      95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                     110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                     125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                     140
Pro Lys Gly Cys Ser
145


<210> 290
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 290
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                      15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                      30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                      45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                      60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                      80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                      95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                     110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                     125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                     140
Pro Lys Gly Cys Ser
145


<210> 291
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 291
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                      15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                      30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                      45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                      60
```

Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 292
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 292
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 293
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 293
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser

```
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 294
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 294

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 295
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 295

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
```

Pro Lys Gly Cys Ser
145

<210> 296
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 296
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 297
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 297
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 298

<211> 149
<212> PRT
<213> human metapneumo virus

<400> 298
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1   5   10   15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20   25   30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35   40   45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50   55   60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65   70   75   80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85   90   95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100   105   110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115   120   125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130   135   140
Pro Lys Gly Cys Ser
145

<210> 299
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 299
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1   5   10   15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20   25   30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35   40   45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50   55   60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65   70   75   80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85   90   95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100   105   110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115   120   125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130   135   140
Pro Lys Gly Cys Ser
145

<210> 300
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 300

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 301
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 301

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 302
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 302

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
```

35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 303
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 303
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 304
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 304
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80

```
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 305
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 305

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 306
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 306

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
```

```
        115                     120                     125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                     135                     140
Pro Lys Gly Cys Ser
145
```

<210> 307
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 307

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 308
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 308

```
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
 1               5                  10                  15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 309
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 309
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1   5   10   15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20   25   30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35   40   45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50   55   60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65   70   75   80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85   90   95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100   105   110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115   120   125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130   135   140
Pro Lys Gly Cys Ser
145

<210> 310
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 310
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1   5   10   15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20   25   30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35   40   45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50   55   60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65   70   75   80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85   90   95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100   105   110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115   120   125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130   135   140
Pro Lys Gly Cys Ser
145

<210> 311
<211> 149
<212> PRT

<213> human metapneumo virus

<400> 311
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 312
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 312
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
20 25 30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
35 40 45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
50 55 60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65 70 75 80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
85 90 95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
100 105 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
115 120 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
130 135 140
Pro Lys Gly Cys Ser
145

<210> 313
<211> 149
<212> PRT
<213> human metapneumo virus

<400> 313
Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln Leu Pro Ile
1 5 10 15

```
Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala Ala Pro Ser
            20                  25                  30
Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg Glu Asp Gln
        35                  40                  45
Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr Pro Asn Glu
    50                  55                  60
Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp Thr Ala Ala
65                  70                  75                  80
Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile Asn Ile Ser
                85                  90                  95
Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His Pro Ile Ser
            100                 105                 110
Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys Tyr Lys Gly
        115                 120                 125
Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile Lys Gln Leu
    130                 135                 140
Pro Lys Gly Cys Ser
145
```

<210> 314
<211> 539
<212> PRT
<213> human metapneumo virus

<400> 314

```
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ala Asp Gly Pro
    50                  55                  60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80
Leu Arg Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95
Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125
Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Lys Thr
    130                 135                 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175
Ile Asn Lys Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser
            180                 185                 190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220
Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
```

275 280 285
Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
340 345 350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385 390 395 400
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
435 440 445
Val Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465 470 475 480
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
485 490 495
Leu Ile Ala Val Leu Gly Ser Thr Met Ile Leu Val Ser Val Phe Ile
500 505 510
Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
515 520 525
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
530 535

<210> 315
<211> 539
<212> PRT
<213> human metapneumo virus

<400> 315
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1 5 10 15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50 55 60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85 90 95
Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
165 170 175
Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225 230 235 240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Thr Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
275 280 285
Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
340 345 350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385 390 395 400
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
435 440 445
Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465 470 475 480
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
485 490 495
Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
500 505 510
Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
515 520 525
Gly Val Thr Asn Asn Gly Phe Ile Pro His Ser
530 535

<210> 316
<211> 539
<212> PRT
<213> human metapneumo virus

<400> 316
Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln
1 5 10 15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe

35 40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
50 55 60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85 90 95
Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Ile Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu Lys Gln Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160
Ala Val Arg Glu Leu Lys Glu Phe Val Ser Lys Asn Leu Thr Ser Ala
165 170 175
Ile Asn Arg Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Ala Arg Ala Val Ser Tyr Met Pro Thr Ser Ala Gly Gln
225 230 235 240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala
275 280 285
Ala Pro Ser Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile
340 345 350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Trp Val Gly Ile Ile
385 390 395 400
Lys Gln Leu Pro Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
435 440 445
Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Lys Ile
465 470 475 480
Leu Asn Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Val Ile
485 490 495
Leu Val Ala Val Leu Gly Leu Thr Met Ile Ser Val Ser Ile Ile Ile
500 505 510
Ile Ile Lys Lys Thr Arg Lys Pro Thr Gly Ala Pro Pro Glu Leu Asn
515 520 525

```
Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser
    530                 535
```

<210> 317
<211> 539
<212> PRT
<213> human metapneumo virus

<400> 317

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Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
    50                  55                  60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95
Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Ile Ala Ile Ala Lys Thr Ile
        115                 120                 125
Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu Lys Thr Thr
    130                 135                 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160
Ala Val Arg Glu Leu Lys Glu Phe Val Ser Lys Asn Leu Thr Ser Ala
                165                 170                 175
Ile Asn Lys Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser
            180                 185                 190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220
Ala Glu Leu Ala Arg Ala Val Ser Tyr Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala
        275                 280                 285
Ala Pro Ser Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300
Glu Asp Gln Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile
            340                 345                 350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400
Lys Gln Leu Pro Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
```

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                405                     410                     415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                     425                     430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                     440                     445
Ile Arg Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                     455                     460
Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Lys Ile
465                     470                     475                     480
Leu Asn Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
                485                     490                     495
Leu Ile Ala Val Leu Gly Leu Thr Met Ile Ser Val Ser Ile Ile Ile
            500                     505                     510
Ile Ile Lys Lys Thr Arg Lys Pro Thr Gly Ala Pro Pro Glu Leu Asn
        515                     520                     525
Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser
    530                     535
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```
<210> 318
<211> 1620
<212> DNA
<213> human metapneumo virus

<400> 318
atgtcttgga aagtggtgat catttttttca ttgttaataa cacctcaaca cggtcttaaa 60
gagagctact tagaagagtc atgtagcact ataactgaag gatatctcag tgttctgagg 120
acaggttggt acaccaatgt ttttacactg gaggtaggcg atgtagagaa ccttacatgt 180
gccgatggac ccagcttaat aaaaacagaa ttagacctga ccaaaagtgc actaagagag 240
ctcagaacag tttctgctga tcaactggca agagaggagc aaattgaaaa tcccagacaa 300
tctagattcg ttctaggagc aatagcactc ggtgttgcaa ctgcagctgc agttacagca 360
ggtgttgcaa ttgccaaaac catccggctt gaaagtgaag taacagcaat taagaatgcc 420
ctcaaaaaga ccaatgaagc agtatctaca ttggggaatg gagttcgtgt gttggcaact 480
gcagtgagag agctgaaaga ttttgtgagc aagaatctaa cacgtgcaat caacaaaaac 540
aagtgcgaca ttgctgacct gaaaatggcc gttagcttca gtcaattcaa cagaaggttc 600
ctaaatgttg tgcggcaatt ttcagacaac gctggaataa caccagcaat atctttggac 660
ttaatgacag atgctgaact agccagagct gtttccaaca tgccaacatc tgcaggacaa 720
ataaaactga tgttggagaa ccgtgcaatg gtaagaagaa aagggttcgg aatcctgata 780
ggagtttacg gaagctccgt aatttacatg gtgcaactgc caatctttgg ggttatagac 840
acgccttgct ggatagtaaa agcagcccct tcttgttcag gaaaaaaggg aaactatgct 900
tgcctcttaa gagaagacca aggatggtat tgtcaaaatg cagggtcaac tgtttactac 960
ccaaatgaaa aagactgtga aacaagagga gaccatgtct tttgcgacac agcagcagga 1020
atcaatgttg ctgagcagtc aaaggagtgc aacataaaca tatctactac taattaccca 1080
tgcaaagtta gcacaggaag acatcctatc agtatggttg cactatctcc tcttggggct 1140
ttggttgctt gctacaaggg agtgagctgt tccattggca gcaacagagt agggatcatc 1200
aagcaactga acaaaggctg ctcttatata accaaccaag acgcagacac agtgacaata 1260
gacaacactg tataccagct aagcaaagtt gaaggcgaac agcatgttat aaaaggaagg 1320
ccagtgtcaa gcagctttga cccagtcaag tttcctgaag atcaattcaa tgttgcactt 1380
gaccaagttt tcgagagcat tgagaacagt caggccttgg tggatcaatc aaacagaatc 1440
ctaagcagtg cagagaaagg aaacactggc ttcatcattg taataattct aattgctgtc 1500
cttggctcta ccatgatcct agtgagtgtt tttatcataa taaagaaaac aaagaaaccc 1560
acaggagcac ctccagagct gagtggtgtc acaaacaatg gcttcatacc acataattag 1620

<210> 319
<211> 1620
<212> DNA
<213> human metapneumo virus

<400> 319
atgtcttgga aagtggtgat catttttttca ttgctaataa cacctcaaca cggtcttaaa 60
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gagagctacc tagaagaatc atgtagcact ataactgagg gatatcttag tgttctgagg 120
acaggttggt ataccaacgt ttttacatta gaggtgggtg atgtagaaaa ccttacatgt 180
tctgatggac ctagcctaat aaaaacagaa ttagatctga ccaaaagtgc actaagagag 240
ctcaaaacag tctctgctga ccaattggca agagaggaac aaattgagaa tcccagacaa 300
tctaggtttg ttctaggagc aatagcactc ggtgttgcaa cagcagctgc agtcacagca 360
ggtgttgcaa ttgccaaaac catccggctt gagagtgaag tcacagcaat taagaatgcc 420
ctcaaaacga ccaatgaagc agtatctaca ttggggaatg gagttcgagt gttggcaact 480
gcagtgagag agctaaaaga ctttgtgagc aagaatttaa ctcgtgcaat caacaaaaac 540
aagtgcgaca ttgatgacct aaaaatggct gttagcttca gtcaattcaa cagaaggttt 600
ctaaatgttg tgcggcaatt ttcagacaat gctggaataa caccagcaat atctttggac 660
ttaatgacag atgctgaact agccagggcc gtttctaaca tgccgacatc tgcaggacaa 720
ataaaattga tgttggagaa ccgtgcgatg gtgcgaagaa aggggttcgg aatcctgata 780
ggggtctacg ggagctccgt aatttacacg gtgcagctgc caatctttgg cgttatagac 840
acgccttgct ggatagtaaa agcagcccct tcttgttccg aaaaaaaggg aaactatgct 900
tgcctcttaa gagaagacca agggtggtat tgtcagaatg cagggtcaac tgtttactac 960
ccaaatgaga aagactgtga aacaagagga gaccatgtct tttgcgacac agcagcagga 1020
attaatgttg ctgagcaatc aaaggagtgc aacatcaaca tatccactac aaattaccca 1080
tgcaaagtca gcacaggaag acatcctatc agtatggttg cactgtctcc tcttggggct 1140
ctggttgctt gctacaaagg agtaagctgt tccattggca gcaacagagt agggatcatc 1200
aagcagctga acaaaggttg ctcctatata accaaccaag atgcagacac agtgacaata 1260
gacaacactg tatatcagct aagcaaagtt gagggtgaac agcatgttat aaaaggcaga 1320
ccagtgtcaa gcagctttga tccaatcaag tttcctgaag atcaattcaa tgttgcactt 1380
gaccaagttt ttgagaacat tgaaaacagc caggccttag tagatcaatc aaacagaatc 1440
ctaagcagtg cagagaaagg gaatactggc tttatcattg taataattct aattgctgtc 1500
cttggctcta gcatgatcct agtgagcatc ttcattataa tcaagaaaac aaagaaacca 1560
acgggagcac ctccagagct gagtggtgtc acaaacaatg gcttcatacc acacagttag 1620

<210> 320
<211> 1620
<212> DNA
<213> human metapneumo virus

<400> 320
atgtcttgga aagtgatgat catcatttcg ttactcataa caccccagca cgggctaaag 60
gagagttatt tggaagaatc atgtagtact ataactgagg gatacctcag tgttttaaga 120
acaggctggt acactaatgt cttcacatta gaagttggtg atgttgaaaa tcttacatgt 180
actgatggac ctagcttaat caaaacagaa cttgatctaa caaaaagtgc tttaagggaa 240
ctcaaaacag tctctgctga tcagttggcg agagaggagc aaattgaaaa tcccagacaa 300
tcaagatttg tcttaggtgc gatagctctc ggagttgcta cagcagcagc agtcacagca 360
ggcattgcaa tagccaaaac cataaggctt gagagtgagg tgaatgcaat taaaggtgct 420
ctcaaacaaa ctaatgaagc agtatccaca ttagggaatg gtgtgcgggt cctagccact 480
gcagtgagag agctaaaaga atttgtgagc aaaaacctga ctagtgcaat caacaggaac 540
aaatgtgaca ttgctgatct gaagatggct gtcagcttca gtcaattcaa cagaagattt 600
ctaaatgttg tgcggcagtt ttcagacaat gcagggataa caccagcaat atcattggac 660
ctgatgactg atgctgagtt ggccagagct gtatcataca tgccaacatc tgcagggcag 720
ataaaactga tgttggagaa ccgcgcaatg gtaaggagaa aaggatttgg aatcctgata 780
ggggtctacg gaagctctgt gatttacatg gttcaattgc cgatctttgg tgtcatagat 840
acaccttgtt ggatcatcaa ggcagctccc tcttgctcag aaaaaaacgg gaattatgct 900
tgcctcctaa gagaggatca agggtggtat tgtaaaaatg caggatctac tgtttactac 960
ccaaatgaaa aagactgcga aacaagaggt gatcatgttt tttgtgacac agcagcaggg 1020
atcaatgttg ctgagcaatc aagagaatgc aacatcaaca tatctactac caactaccca 1080
tgcaaagtca gcacaggaag acaccctata agcatggttg cactatcacc tctcggtgct 1140
ttggtggctt gctataaagg ggtaagctgc tcgattggca gcaattgggt tggaatcatc 1200
aaacaattac ccaaaggctg ctcatacata accaaccagg atgcagacac tgtaacaatt 1260
gacaataccg tgtatcaact aagcaaagtt gaaggtgaac agcatgtaat aaaagggaga 1320
ccagtttcaa gcagttttga tccaatcaag tttcctgagg atcagttcaa tgttgcgctt 1380
gatcaagtct tcgaaagcat tgagaacagt caggcactag tggaccagtc aaacaaaatt 1440
ctaaacagtg cagaaaaagg aaacactggt ttcattatcg tagtaatttt ggttgctgtt 1500
cttggtctaa ccatgatttc agtgagcatc atcatcataa tcaagaaaac aaggaagccc 1560
acaggagcac ctccagagct gaatggtgtc accaacggcg gtttcatacc acatagttag 1620

<210> 321
<211> 1620
<212> DNA
<213> human metapneumo virus

<400> 321
atgtcttgga aagtgatgat tatcatttcg ttactcataa cacctcagca cggactaaaa 60
gaaagttatt tagaagaatc atgtagtact ataactgaag gatatctcag tgttttaaga 120
acaggttggt acaccaatgt ctttacatta gaagttggtg atgttgaaaa tcttacatgt 180
actgatggac ctagcttaat caaaacagaa cttgacctaa ccaaaagtgc tctgagagaa 240
ctcaaaacag tttctgctga tcagttagcg agagaagaac aaattgaaaa tcccagacaa 300
tcaaggtttg tcctaggtgc aatagctctt ggagttgcca cagcagcagc agtcacagca 360
ggcattgcaa tagccaaaac cataagactt gagagtgaag tgaatgcaat caaaggtgct 420
ctcaaaacaa ccaacgaggc agtatccaca ctaggaaatg gagtgcgagt cctagccact 480
gcagtaagag agctgaaaga atttgtgagc aaaaacctga ctagtgcgat caacaagaac 540
aaatgtgaca ttgctgatct gaagatggct gtcagcttca gtcaattcaa cagaagattc 600
ctaaatgttg tgcggcagtt ttcagacaat gcagggataa caccagcaat atcattggac 660
ctaatgactg atgctgagct ggccagagct gtatcataca tgccaacatc tgcaggacag 720
ataaaactaa tgttagagaa ccgtgcaatg gtgaggagaa aaggatttgg aatcttgata 780
ggggtctacg gaagctctgt gatttacatg gtccagctgc cgatctttgg tgtcatagat 840
acaccttgtt ggataatcaa ggcagctccc tcttgttcag aaaaagatgg aaattatgct 900
tgcctcctaa gagaggatca agggtggtat tgcaaaaatg caggatccac tgtttactac 960
ccaaatgaaa aagactgcga aacaagaggt gatcatgttt tttgtgacac agcagcaggg 1020
atcaatgttg ctgagcaatc aagagaatgc aacatcaaca tatctaccac caactaccca 1080
tgcaaagtca gcacaggaag acaccctatc agcatggttg cactatcacc tctcggtgct 1140
ttggtagctt gctacaaggg ggttagctgc tcgattggca gtaatcgggt tggaataatc 1200
aaacaactac ctaaaggctg ctcatacata actaaccagg acgcagacac tgtaacaatt 1260
gacaacactg tgtatcaact aagcaaagtt gagggtgaac agcatgtaat aaaaggagga 1320
ccagtttcaa gcagttttga tccaatcagg tttcctgagg atcagttcaa tgttgcgctt 1380
gatcaagtct ttgaaagcat tgaaaacagt caagcactag tggaccagtc aaacaaaatt 1440
ctgaacagtg cagaaaaagg aaacactggt ttcattattg taataatttt gattgctgtt 1500
cttgggttaa ccatgatttc agtgagcatc atcatcataa tcaaaaaaac aaggaagccc 1560
acaggggcac ctccagagct gaatggtgtt accaacggcg gttttatacc gcatagttag 1620

<210> 322
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 322
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1   5   10   15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
            20   25   30
Leu Val Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
        35   40   45
Leu Ile Ile Asn Tyr Lys Met Gln Lys Asn Thr Ser Glu Ser Glu His
    50   55   60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65   70   75   80
Pro Thr Asp Asn Ser Asp Thr Asn Ser Ser Pro Gln His Pro Thr Gln
                85   90   95
Gln Ser Thr Glu Gly Ser Thr Leu Tyr Phe Ala Ala Ser Ala Ser Ser
            100   105   110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Asn Arg Pro Pro
        115   120   125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Lys Thr
    130   135   140

Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Thr Ser Ser Arg Thr
145 150 155 160
His Ser Pro Pro Arg Ala Thr Thr Arg Thr Ala Arg Arg Thr Thr Thr
165 170 175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
180 185 190
Pro Asp Ile Ser Ala Thr Thr His Lys Asn Glu Glu Ala Ser Pro Ala
195 200 205
Ser Pro Gln Thr Ser Ala Ser Thr Thr Arg Ile Gln Arg Lys Ser Val
210 215 220
Glu Ala Asn Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225 230 235

<210> 323
<211> 219
<212> PRT
<213> human metapneumo virus

<400> 323
Met Glu Val Lys Val Glu Asn Ile Arg Ala Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Ile Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Thr Ile Gln Lys Thr Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Pro Pro Thr Glu Pro Asn Lys Glu Ala Ser Thr Ile
65 70 75 80
Ser Thr Asp Asn Pro Asp Ile Asn Pro Ser Ser Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Asn Pro Thr Leu Asn Pro Ala Ala Ser Ala Ser Pro
100 105 110
Ser Glu Thr Glu Pro Ala Ser Thr Pro Asp Thr Thr Asn Arg Leu Ser
115 120 125
Ser Val Asp Arg Ser Thr Ala Gln Pro Ser Glu Ser Arg Thr Lys Thr
130 135 140
Lys Pro Thr Val His Thr Ile Asn Asn Pro Asn Thr Ala Ser Ser Thr
145 150 155 160
Gln Ser Pro Pro Arg Thr Thr Thr Lys Ala Ile Arg Arg Ala Thr Thr
165 170 175
Phe Arg Met Ser Ser Thr Gly Lys Arg Pro Thr Thr Thr Leu Val Gln
180 185 190
Ser Asp Ser Ser Thr Thr Thr Gln Asn His Glu Glu Thr Gly Ser Ala
195 200 205
Asn Pro Gln Ala Ser Ala Ser Thr Met Gln Asn
210 215

<210> 324
<211> 224
<212> PRT
<213> human metapneumo virus

<400> 324
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
1 5 10 15
Lys Ile Lys Asn Arg Ile Arg Ser Ser Arg Cys Tyr Arg Asn Ala Thr
20 25 30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe

```
        35                      40                      45
Leu Ile Ile Asp His Ala Thr Leu Arg Asn Met Ile Lys Thr Glu Asn
    50                      55                      60
Cys Ala Asn Met Pro Ser Ala Glu Pro Ser Lys Lys Thr Pro Met Thr
65                      70                      75                  80
Ser Thr Ala Gly Pro Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
                85                      90                      95
Trp Thr Thr Glu Asn Ser Thr Ser Pro Val Ala Thr Pro Glu Gly His
            100                     105                     110
Pro Tyr Thr Gly Thr Thr Gln Thr Ser Asp Thr Thr Ala Pro Gln Gln
        115                     120                     125
Thr Thr Asp Lys His Thr Ala Pro Leu Lys Ser Thr Asn Glu Gln Ile
    130                     135                     140
Thr Gln Thr Thr Thr Glu Lys Lys Thr Ile Arg Ala Thr Thr Gln Lys
145                     150                     155                 160
Arg Glu Lys Gly Lys Glu Asn Thr Asn Gln Thr Thr Ser Thr Ala Ala
                165                     170                     175
Thr Gln Thr Thr Asn Thr Thr Asn Gln Ile Arg Asn Ala Ser Glu Thr
            180                     185                     190
Ile Thr Thr Ser Asp Arg Pro Arg Thr Asp Thr Thr Thr Gln Ser Ser
        195                     200                     205
Glu Gln Thr Thr Arg Ala Thr Asp Pro Ser Ser Pro Pro His His Ala
    210                     215                     220


<210> 325
<211> 236
<212> PRT
<213> human metapneumo virus

<400> 325
Met Glu Val Arg Val Glu Asn Ile Arg Ala Ile Asp Met Phe Lys Ala
 1               5                  10                  15
Lys Met Lys Asn Arg Ile Arg Ser Ser Lys Cys Tyr Arg Asn Ala Thr
            20                  25                  30
Leu Ile Leu Ile Gly Leu Thr Ala Leu Ser Met Ala Leu Asn Ile Phe
        35                  40                  45
Leu Ile Ile Asp Tyr Ala Met Leu Lys Asn Met Thr Lys Val Glu His
    50                  55                  60
Cys Val Asn Met Pro Pro Val Glu Pro Ser Lys Lys Thr Pro Met Thr
65                  70                  75                  80
Ser Ala Val Asp Leu Asn Thr Lys Pro Asn Pro Gln Gln Ala Thr Gln
                85                  90                  95
Leu Ala Ala Glu Asp Ser Thr Ser Leu Ala Ala Thr Ser Glu Asp His
            100                 105                 110
Leu His Thr Gly Thr Thr Pro Thr Pro Asp Ala Thr Val Ser Gln Gln
        115                 120                 125
Thr Thr Asp Glu Tyr Thr Thr Leu Leu Arg Ser Thr Asn Arg Gln Thr
    130                 135                 140
Thr Gln Thr Thr Thr Glu Lys Lys Pro Thr Gly Ala Thr Thr Lys Lys
145                 150                 155                 160
Glu Thr Thr Thr Arg Thr Thr Ser Thr Ala Ala Thr Gln Thr Leu Asn
                165                 170                 175
Thr Thr Asn Gln Thr Ser Tyr Val Arg Glu Ala Thr Thr Thr Ser Ala
            180                 185                 190
Arg Ser Arg Asn Ser Ala Thr Thr Gln Ser Ser Asp Gln Thr Thr Gln
        195                 200                 205
Ala Ala Asp Pro Ser Ser Gln Pro His His Thr Gln Lys Ser Thr Thr
    210                 215                 220
Thr Thr Tyr Asn Thr Asp Thr Ser Ser Pro Ser Ser
225                 230                 235
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<210> 326
<211> 708
<212> DNA
<213> human metapneumo virus

<400> 326
gaggtgaaag tggagaacat tcgaacaata gatatgctca aagcaagagt aaaaaatcgt 60
gtggcacgca gcaaatgctt taaaaatgcc tctttggtcc tcataggaat aactacattg 120
agtattgccc tcaatatcta tctgatcata aactataaaa tgcaaaaaaa cacatctgaa 180
tcagaacatc acaccagctc atcacccatg gaatccagca gagaaactcc aacggtcccc 240
acagacaact cagacaccaa ctcaagccca cagcatccaa ctcaacagtc cacagaaggc 300
tccacactct actttgcagc ctcagcaagc tcaccagaga cagaaccaac atcaacacca 360
gatacaacaa accgcccgcc cttcgtcgac acacacacaa caccaccaag cgcaagcaga 420
acaaagacaa gtccggcagt ccacacaaaa aacaacccaa ggacaagctc tagaacacat 480
tctccaccac gggcaacgac aaggacggca cgcagaacca ccactctccg cacaagcagc 540
acaagaaaga gaccgtccac agcatcagtc caacctgaca tcagcgcaac aacccacaaa 600
aacgaagaag caagtccagc gagcccacaa acatctgcaa gcacaacaag aatacaaagg 660
aaaagcgtgg aggccaacac atcaacaaca tacaaccaaa ctagttaa 708

<210> 327
<211> 660
<212> DNA
<213> human metapneumo virus

<400> 327
atggaggtga aagtagagaa cattcgagca atagacatgc tcaaagcaag agtgaaaaat 60
cgtgtggcac gtagcaaatg ctttaaaaat gcttctttaa tcctcatagg aataactaca 120
ctgagtatag ctctcaatat ctatctgatc ataaactaca caatacaaaa aaccacatcc 180
gaatcagaac accacaccag ctcaccaccc acagaaccca acaaggaagc ttcaacaatc 240
tccacagaca acccagacat caatccaagc tcacagcatc caactcaaca gtccacagaa 300
aaccccacac tcaaccccgc agcatcagcg agcccatcag aaacagaacc agcatcaaca 360
ccagacacaa caaaccgcct gtcctccgta gacaggtcca cagcacaacc aagtgaaagc 420
agaacaaaga caaaaccgac agtccacaca atcaacaacc caaacacagc ttccagtaca 480
caatccccac cacggacaac aacgaaggca atccgcagag ccaccacttt ccgcatgagc 540
agcacaggaa aaagaccaac cacaacatta gtccagtccg acagcagcac cacaacccaa 600
aatcatgaag aaacaggttc agcgaaccca caggcgtctg caagcacaat gcaaaactag 660

<210> 328
<211> 675
<212> DNA
<213> human metapneumo virus

<400> 328
atggaagtaa gagtggagaa cattcgagcg atagacatgt tcaaagcaaa gataaaaaac 60
cgtataagaa gcagcaggtg ctatagaaat gctacactga tccttattgg actaacagcg 120
ttaagcatgg cacttaatat tttcctgatc atcgatcatg caacattaag aaacatgatc 180
aaaacagaaa actgtgctaa catgccgtcg gcagaaccaa gcaaaaagac cccaatgacc 240
tccacagcag gcccaaacac caaacccaat ccacagcaag caacacagtg gaccacagag 300
aactcaacat ccccagtagc aaccccagag ggccatccat acacagggac aactcaaaca 360
tcagacacaa cagctcccca gcaaaccaca gacaaacaca cagcaccgct aaaatcaacc 420
aatgaacaga tcacccagac aaccacagag aaaaagacaa tcagagcaac aacccaaaaa 480
agggaaaaag gaaaagaaaa cacaaaccaa accacaagca cagctgcaac ccaaacaacc 540
aacaccacca accaaatcag aaatgcaagt gagacaatca caacatccga cagacccaga 600
actgacacca caacccaaag cagcgaacag acaacccggg caacagaccc aagctcccca 660
ccacaccatg catag 675

<210> 329
<211> 711

<212> DNA
<213> human metapneumo virus

<400> 329
atggaagtaa gagtggagaa cattcgggca atagacatgt tcaaagcaaa aatgaaaaac 60
cgtataagaa gtagcaagtg ctatagaaat gctacactga tccttattgg attaacagca 120
ttaagtatgg cacttaatat ttttttaatc attgattatg caatgttaaa aaacatgacc 180
aaagtggaac actgtgttaa tatgccgccg gtagaaccaa gcaagaagac cccaatgacc 240
tctgcagtag acttaaacac caaacccaat ccacagcagg caacacagtt ggccgcagag 300
gattcaacat ctctagcagc aacctcagag gaccatctac acacagggac aactccaaca 360
ccagatgcaa cagtctctca gcaaaccaca gacgagtaca caacattgct gagatcaacc 420
aacagacaga ccacccaaac aaccacagag aaaaagccaa ccggagcaac aaccaaaaaa 480
gaaaccacaa ctcgaactac aagcacagct gcaacccaaa cactcaacac taccaaccaa 540
actagctatg tgagagaggc aaccacaaca tccgccagat ccagaaacag tgccacaact 600
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<213> human metapneumo virus

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35 40 45
Ala Ile Glu Asn Pro Val Ile Glu His Val Arg Leu Lys Asn Ala Val
50 55 60
Asn Ser Lys Met Lys Ile Ser Asp Tyr Lys Ile Val Glu Pro Val Asn
65 70 75 80
Met Gln His Glu Ile Met Lys Asn Val His Ser Cys Glu Leu Thr Leu
85 90 95
Leu Lys Gln Phe Leu Thr Arg Ser Lys Asn Ile Ser Thr Leu Lys Leu
100 105 110
Asn Met Ile Cys Asp Trp Leu Gln Leu Lys Ser Thr Ser Asp Asp Thr
115 120 125
Ser Ile Leu Ser Phe Ile Asp Val Glu Phe Ile Pro Ser Trp Val Ser
130 135 140
Asn Trp Phe Ser Asn Trp Tyr Asn Leu Asn Lys Leu Ile Leu Glu Phe
145 150 155 160
Arg Lys Glu Glu Val Ile Arg Thr Gly Ser Ile Leu Cys Arg Ser Leu
165 170 175
Gly Lys Leu Val Phe Val Val Ser Ser Tyr Gly Cys Ile Val Lys Ser
180 185 190
Asn Lys Ser Lys Arg Val Ser Phe Phe Thr Tyr Asn Gln Leu Leu Thr
195 200 205
Trp Lys Asp Val Met Leu Ser Arg Phe Asn Ala Asn Phe Cys Ile Trp
210 215 220
Val Ser Asn Ser Leu Asn Glu Asn Gln Glu Gly Leu Gly Leu Arg Ser
225 230 235 240
Asn Leu Gln Gly Ile Leu Thr Asn Lys Leu Tyr Glu Thr Val Asp Tyr
245 250 255
Met Leu Ser Leu Cys Cys Asn Glu Gly Phe Ser Leu Val Lys Glu Phe
260 265 270
Glu Gly Phe Ile Met Ser Glu Ile Leu Arg Ile Thr Glu His Ala Gln
275 280 285
Phe Ser Thr Arg Phe Arg Asn Thr Leu Leu Asn Gly Leu Thr Asp Gln
290 295 300

Leu Thr Lys Leu Lys Asn Lys Asn Arg Leu Arg Val His Gly Thr Val
305 310 315 320
Leu Glu Asn Asn Asp Tyr Pro Met Tyr Glu Val Val Leu Lys Leu Leu
325 330 335
Gly Asp Thr Leu Arg Cys Ile Lys Leu Leu Ile Asn Lys Asn Leu Glu
340 345 350
Asn Ala Ala Glu Leu Tyr Tyr Ile Phe Arg Ile Phe Gly His Pro Met
355 360 365
Val Asp Glu Arg Asp Ala Met Asp Ala Val Lys Leu Asn Asn Glu Ile
370 375 380
Thr Lys Ile Leu Arg Trp Glu Ser Leu Thr Glu Leu Arg Gly Ala Phe
385 390 395 400
Ile Leu Arg Ile Ile Lys Gly Phe Val Asp Asn Asn Lys Arg Trp Pro
405 410 415
Lys Ile Lys Asn Leu Lys Val Leu Ser Lys Arg Trp Thr Met Tyr Phe
420 425 430
Lys Ala Lys Ser Tyr Pro Ser Gln Leu Glu Leu Ser Glu Gln Asp Phe
435 440 445
Leu Glu Leu Ala Ala Ile Gln Phe Glu Gln Glu Phe Ser Val Pro Glu
450 455 460
Lys Thr Asn Leu Glu Met Val Leu Asn Asp Lys Ala Ile Ser Pro Pro
465 470 475 480
Lys Arg Leu Ile Trp Ser Val Tyr Pro Lys Asn Tyr Leu Pro Glu Lys
485 490 495
Ile Lys Asn Arg Tyr Leu Glu Glu Thr Phe Asn Ala Ser Asp Ser Leu
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Lys Thr Arg Arg Val Leu Glu Tyr Tyr Leu Lys Asp Asn Lys Phe Asp
515 520 525
Gln Lys Glu Leu Lys Ser Tyr Val Val Lys Gln Glu Tyr Leu Asn Asp
530 535 540
Lys Asp His Ile Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser Val
545 550 555 560
Gly Arg Met Phe Ala Met Gln Pro Gly Lys Gln Arg Gln Ile Gln Ile
565 570 575
Leu Ala Glu Lys Leu Leu Ala Asp Asn Ile Val Pro Phe Phe Pro Glu
580 585 590
Thr Leu Thr Lys Tyr Gly Asp Leu Asp Leu Gln Arg Ile Met Glu Ile
595 600 605
Lys Ser Glu Leu Ser Ser Ile Lys Thr Arg Arg Asn Asp Ser Tyr Asn
610 615 620
Asn Tyr Ile Ala Arg Ala Ser Ile Val Thr Asp Leu Ser Lys Phe Asn
625 630 635 640
Gln Ala Phe Arg Tyr Glu Thr Thr Ala Ile Cys Ala Asp Val Ala Asp
645 650 655
Glu Leu His Gly Thr Gln Ser Leu Phe Cys Trp Leu His Leu Ile Val
660 665 670
Pro Met Thr Thr Met Ile Cys Ala Tyr Arg His Ala Pro Pro Glu Thr
675 680 685
Lys Gly Glu Tyr Asp Ile Asp Lys Ile Glu Glu Gln Ser Gly Leu Tyr
690 695 700
Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu Trp Thr
705 710 715 720
Met Glu Ala Ile Ser Leu Leu Asp Val Val Ser Val Lys Thr Arg Cys
725 730 735
Gln Met Thr Ser Leu Leu Asn Gly Asp Asn Gln Ser Ile Asp Val Ser
740 745 750
Lys Pro Val Lys Leu Ser Glu Gly Leu Asp Glu Val Lys Ala Asp Tyr
755 760 765
Ser Leu Ala Val Lys Met Leu Lys Glu Ile Arg Asp Ala Tyr Arg Asn
770 775 780
Ile Gly His Lys Leu Lys Glu Gly Glu Thr Tyr Ile Ser Arg Asp Leu

785 790 795 800
Gln Phe Ile Ser Lys Val Ile Gln Ser Glu Gly Val Met His Pro Thr
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Pro Ile Lys Lys Ile Leu Arg Val Gly Pro Trp Ile Asn Thr Ile Leu
820 825 830
Asp Asp Ile Lys Thr Ser Ala Glu Ser Ile Gly Ser Leu Cys Gln Glu
835 840 845
Leu Glu Phe Arg Gly Glu Ser Ile Ile Val Ser Leu Ile Leu Arg Asn
850 855 860
Phe Trp Leu Tyr Asn Leu Tyr Met His Glu Ser Lys Gln His Pro Leu
865 870 875 880
Ala Gly Lys Gln Leu Phe Lys Gln Leu Asn Lys Thr Leu Thr Ser Val
885 890 895
Gln Arg Phe Phe Glu Ile Lys Lys Glu Asn Glu Val Val Asp Leu Trp
900 905 910
Met Asn Ile Pro Met Gln Phe Gly Gly Gly Asp Pro Val Val Phe Tyr
915 920 925
Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala Ile Ser
930 935 940
His Val Asp Ile Leu Leu Arg Ile Ser Ala Asn Ile Arg Asn Glu Ala
945 950 955 960
Lys Ile Ser Phe Phe Lys Ala Leu Leu Ser Ile Glu Lys Asn Glu Arg
965 970 975
Ala Thr Leu Thr Thr Leu Met Arg Asp Pro Gln Ala Val Gly Ser Glu
980 985 990
Arg Gln Ala Lys Val Thr Ser Asp Ile Asn Arg Thr Ala Val Thr Ser
995 1000 1005
Ile Leu Ser Leu Ser Pro Asn Gln Leu Phe Ser Asp Ser Ala Ile His
1010 1015 1020
Tyr Ser Arg Asn Glu Glu Glu Val Gly Ile Ile Ala Asp Asn Ile Thr
1025 1030 1035 1040
Pro Val Tyr Pro His Gly Leu Arg Val Leu Tyr Glu Ser Leu Pro Phe
1045 1050 1055
His Lys Ala Glu Lys Val Val Asn Met Ile Ser Gly Thr Lys Ser Ile
1060 1065 1070
Thr Asn Leu Leu Gln Arg Thr Ser Ala Ile Asn Gly Glu Asp Ile Asp
1075 1080 1085
Arg Ala Val Ser Met Met Leu Glu Asn Leu Gly Leu Leu Ser Arg Ile
1090 1095 1100
Leu Ser Val Val Val Asp Ser Ile Glu Ile Pro Thr Lys Ser Asn Gly
1105 1110 1115 1120
Arg Leu Ile Cys Cys Gln Ile Ser Arg Thr Leu Arg Glu Thr Ser Trp
1125 1130 1135
Asn Asn Met Glu Ile Val Gly Val Thr Ser Pro Ser Ile Thr Thr Cys
1140 1145 1150
Met Asp Val Ile Tyr Ala Thr Ser Ser His Leu Lys Gly Ile Ile Ile
1155 1160 1165
Glu Lys Phe Ser Thr Asp Arg Thr Thr Arg Gly Gln Arg Gly Pro Lys
1170 1175 1180
Ser Pro Trp Val Gly Ser Ser Thr Gln Glu Lys Lys Leu Val Pro Val
1185 1190 1195 1200
Tyr Asn Arg Gln Ile Leu Ser Lys Gln Gln Arg Glu Gln Leu Glu Ala
1205 1210 1215
Ile Gly Lys Met Arg Trp Val Tyr Lys Gly Thr Pro Gly Leu Arg Arg
1220 1225 1230
Leu Leu Asn Lys Ile Cys Leu Gly Ser Leu Gly Ile Ser Tyr Lys Cys
1235 1240 1245
Val Lys Pro Leu Leu Pro Arg Phe Met Ser Val Asn Phe Leu His Arg
1250 1255 1260
Leu Ser Val Ser Ser Arg Pro Met Glu Phe Pro Ala Ser Val Pro Ala
1265 1270 1275 1280

Tyr Arg Thr Thr Asn Tyr His Phe Asp Thr Ser Pro Ile Asn Gln Ala
1285 1290 1295
Leu Ser Glu Arg Phe Gly Asn Glu Asp Ile Asn Leu Val Phe Gln Asn
1300 1305 1310
Ala Ile Ser Cys Gly Ile Ser Ile Met Ser Val Val Glu Gln Leu Thr
1315 1320 1325
Gly Arg Ser Pro Lys Gln Leu Val Leu Ile Pro Gln Leu Glu Glu Ile
1330 1335 1340
Asp Ile Met Pro Pro Pro Val Phe Gln Gly Lys Phe Asn Tyr Lys Leu
1345 1350 1355 1360
Val Asp Lys Ile Thr Ser Asp Gln His Ile Phe Ser Pro Asp Lys Ile
1365 1370 1375
Asp Met Leu Thr Leu Gly Lys Met Leu Met Pro Thr Ile Lys Gly Gln
1380 1385 1390
Lys Thr Asp Gln Phe Leu Asn Lys Arg Glu Asn Tyr Phe His Gly Asn
1395 1400 1405
Asn Leu Ile Glu Ser Leu Ser Ala Ala Leu Ala Cys His Trp Cys Gly
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Ile Leu Thr Glu Gln Cys Ile Glu Asn Asn Ile Phe Lys Lys Asp Trp
1425 1430 1435 1440
Gly Asp Gly Phe Ile Ser Asp His Ala Phe Met Asp Phe Lys Ile Phe
1445 1450 1455
Leu Cys Val Phe Lys Thr Lys Leu Leu Cys Ser Trp Gly Ser Gln Gly
1460 1465 1470
Lys Asn Ile Lys Asp Glu Asp Ile Val Asp Glu Ser Ile Asp Lys Leu
1475 1480 1485
Leu Arg Ile Asp Asn Thr Phe Trp Arg Met Phe Ser Lys Val Met Phe
1490 1495 1500
Glu Ser Lys Val Lys Lys Arg Ile Met Leu Tyr Asp Val Lys Phe Leu
1505 1510 1515 1520
Ser Leu Val Gly Tyr Ile Gly Phe Lys Asn Trp Phe Ile Glu Gln Leu
1525 1530 1535
Arg Ser Ala Glu Leu His Glu Val Pro Trp Ile Val Asn Ala Glu Gly
1540 1545 1550
Asp Leu Val Glu Ile Lys Ser Ile Lys Ile Tyr Leu Gln Leu Ile Glu
1555 1560 1565
Gln Ser Leu Phe Leu Arg Ile Thr Val Leu Asn Tyr Thr Asp Met Ala
1570 1575 1580
His Ala Leu Thr Arg Leu Ile Arg Lys Lys Leu Met Cys Asp Asn Ala
1585 1590 1595 1600
Leu Leu Thr Pro Ile Pro Ser Pro Met Val Asn Leu Thr Gln Val Ile
1605 1610 1615
Asp Pro Thr Glu Gln Leu Ala Tyr Phe Pro Lys Ile Thr Phe Glu Arg
1620 1625 1630
Leu Lys Asn Tyr Asp Thr Ser Ser Asn Tyr Ala Lys Gly Lys Leu Thr
1635 1640 1645
Arg Asn Tyr Met Ile Leu Leu Pro Trp Gln His Val Asn Arg Tyr Asn
1650 1655 1660
Phe Val Phe Ser Ser Thr Gly Cys Lys Val Ser Leu Lys Thr Cys Ile
1665 1670 1675 1680
Gly Lys Leu Met Lys Asp Leu Asn Pro Lys Val Leu Tyr Phe Ile Gly
1685 1690 1695
Glu Gly Ala Gly Asn Trp Met Ala Arg Thr Ala Cys Glu Tyr Pro Asp
1700 1705 1710
Ile Lys Phe Val Tyr Arg Ser Leu Lys Asp Asp Leu Asp His His Tyr
1715 1720 1725
Pro Leu Glu Tyr Gln Arg Val Ile Gly Glu Leu Ser Arg Ile Ile Asp
1730 1735 1740
Ser Gly Glu Gly Leu Ser Met Glu Thr Thr Asp Ala Thr Gln Lys Thr
1745 1750 1755 1760
His Trp Asp Leu Ile His Arg Val Ser Lys Asp Ala Leu Leu Ile Thr

1765 1770 1775
Leu Cys Asp Ala Glu Phe Lys Asp Arg Asp Asp Phe Phe Lys Met Val
1780 1785 1790
Ile Leu Trp Arg Lys His Val Leu Ser Cys Arg Ile Cys Thr Thr Tyr
1795 1800 1805
Gly Thr Asp Leu Tyr Leu Phe Ala Lys Tyr His Ala Lys Asp Cys Asn
1810 1815 1820
Val Lys Leu Pro Phe Phe Val Arg Ser Val Ala Thr Phe Ile Met Gln
1825 1830 1835 1840
Gly Ser Lys Leu Ser Gly Ser Glu Cys Tyr Ile Leu Leu Thr Leu Gly
1845 1850 1855
His His Asn Asn Leu Pro Cys His Gly Glu Ile Gln Asn Ser Lys Met
1860 1865 1870
Lys Ile Ala Val Cys Asn Asp Phe Tyr Ala Ala Lys Lys Leu Asp Asn
1875 1880 1885
Lys Ser Ile Glu Ala Asn Cys Lys Ser Leu Leu Ser Gly Leu Arg Ile
1890 1895 1900
Pro Ile Asn Lys Lys Glu Leu Asn Arg Gln Arg Arg Leu Leu Thr Leu
1905 1910 1915 1920
Gln Ser Asn His Ser Ser Val Ala Thr Val Gly Gly Ser Lys Val Ile
1925 1930 1935
Glu Ser Lys Trp Leu Thr Asn Lys Ala Asn Thr Ile Ile Asp Trp Leu
1940 1945 1950
Glu His Ile Leu Asn Ser Pro Lys Gly Glu Leu Asn Tyr Asp Phe Phe
1955 1960 1965
Glu Ala Leu Glu Asn Thr Tyr Pro Asn Met Ile Lys Leu Ile Asp Asn
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Leu Val Ser Lys Lys
2005

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35 40 45
Ala Ile Glu Asn Pro Val Ile Glu His Val Arg Leu Lys Asn Ala Val
50 55 60
Asn Ser Lys Met Lys Ile Ser Asp Tyr Lys Val Val Glu Pro Val Asn
65 70 75 80
Met Gln His Glu Ile Met Lys Asn Val His Ser Cys Glu Leu Thr Leu
85 90 95
Leu Lys Gln Phe Leu Thr Arg Ser Lys Asn Ile Ser Thr Leu Lys Leu
100 105 110
Asn Met Ile Cys Asp Trp Leu Gln Leu Lys Ser Thr Ser Asp Asp Thr
115 120 125
Ser Ile Leu Ser Phe Ile Asp Val Glu Phe Ile Pro Ser Trp Val Ser
130 135 140
Asn Trp Phe Ser Asn Trp Tyr Asn Leu Asn Lys Leu Ile Leu Glu Phe
145 150 155 160
Arg Arg Glu Glu Val Ile Arg Thr Gly Ser Ile Leu Cys Arg Ser Leu
165 170 175

Gly Lys Leu Val Phe Ile Val Ser Ser Tyr Gly Cys Ile Val Lys Ser
180 185 190
Asn Lys Ser Lys Arg Val Ser Phe Phe Thr Tyr Asn Gln Leu Leu Thr
195 200 205
Trp Lys Asp Val Met Leu Ser Arg Phe Asn Ala Asn Phe Cys Ile Trp
210 215 220
Val Ser Asn Ser Leu Asn Glu Asn Gln Glu Gly Leu Gly Leu Arg Ser
225 230 235 240
Asn Leu Gln Gly Met Leu Thr Asn Lys Leu Tyr Glu Thr Val Asp Tyr
245 250 255
Met Leu Ser Leu Cys Cys Asn Glu Gly Phe Ser Leu Val Lys Glu Phe
260 265 270
Glu Gly Phe Ile Met Ser Glu Ile Leu Arg Ile Thr Glu His Ala Gln
275 280 285
Phe Ser Thr Arg Phe Arg Asn Thr Leu Leu Asn Gly Leu Thr Asp Gln
290 295 300
Leu Thr Lys Leu Lys Asn Lys Asn Arg Leu Arg Val His Gly Thr Val
305 310 315 320
Leu Glu Asn Asn Asp Tyr Pro Met Tyr Glu Val Val Leu Lys Leu Leu
325 330 335
Gly Asp Thr Leu Arg Cys Ile Lys Leu Leu Ile Asn Lys Asn Leu Glu
340 345 350
Asn Ala Ala Glu Leu Tyr Tyr Ile Phe Arg Ile Phe Gly His Pro Met
355 360 365
Val Asp Glu Arg Asp Ala Met Asp Ala Val Lys Leu Asn Asn Glu Ile
370 375 380
Thr Lys Ile Leu Arg Leu Glu Ser Leu Thr Glu Leu Arg Gly Ala Phe
385 390 395 400
Ile Leu Arg Ile Ile Lys Gly Phe Val Asp Asn Asn Lys Arg Trp Pro
405 410 415
Lys Ile Lys Asn Leu Ile Val Leu Ser Lys Arg Trp Thr Met Tyr Phe
420 425 430
Lys Ala Lys Asn Tyr Pro Ser Gln Leu Glu Leu Ser Glu Gln Asp Phe
435 440 445
Leu Glu Leu Ala Ala Ile Gln Phe Glu Gln Glu Phe Ser Val Pro Glu
450 455 460
Lys Thr Asn Leu Glu Met Val Leu Asn Asp Lys Ala Ile Ser Pro Pro
465 470 475 480
Lys Arg Leu Ile Trp Ser Val Tyr Pro Lys Asn Tyr Leu Pro Glu Thr
485 490 495
Ile Lys Asn Arg Tyr Leu Glu Glu Thr Phe Asn Ala Ser Asp Ser Leu
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Lys Thr Arg Arg Val Leu Glu Tyr Tyr Leu Lys Asp Asn Lys Phe Asp
515 520 525
Gln Lys Glu Leu Lys Ser Tyr Val Val Arg Gln Glu Tyr Leu Asn Asp
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Lys Glu His Ile Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser Val
545 550 555 560
Gly Arg Met Phe Ala Met Gln Pro Gly Lys Gln Arg Gln Ile Gln Ile
565 570 575
Leu Ala Glu Lys Leu Leu Ala Asp Asn Ile Val Pro Phe Phe Pro Glu
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Thr Leu Thr Lys Tyr Gly Asp Leu Asp Leu Gln Arg Ile Met Glu Ile
595 600 605
Lys Ser Glu Leu Ser Ser Ile Lys Thr Arg Arg Asn Asp Ser Tyr Asn
610 615 620
Asn Tyr Ile Ala Arg Ala Ser Ile Val Thr Asp Leu Ser Lys Phe Asn
625 630 635 640
Gln Ala Phe Arg Tyr Glu Thr Thr Ala Ile Cys Ala Asp Val Ala Asp
645 650 655
Glu Leu His Gly Thr Gln Ser Leu Phe Cys Trp Leu His Leu Ile Val

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Pro Met Thr Thr Met Ile Cys Ala Tyr Arg His Ala Pro Pro Glu Thr
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Lys Gly Glu Tyr Asp Ile Asp Lys Ile Glu Glu Gln Ser Gly Leu Tyr
    690                     695                     700
Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu Trp Thr
705                     710                     715                 720
Met Glu Ala Ile Ser Leu Leu Asp Val Val Ser Val Lys Thr Arg Cys
                725                     730                     735
Gln Met Thr Ser Leu Leu Asn Gly Asp Asn Gln Ser Ile Asp Val Ser
            740                     745                     750
Lys Pro Val Lys Leu Ser Glu Gly Leu Asp Glu Val Lys Ala Asp Tyr
        755                     760                     765
Arg Leu Ala Ile Lys Met Leu Lys Glu Ile Arg Asp Ala Tyr Arg Asn
    770                     775                     780
Ile Gly His Lys Leu Lys Glu Gly Glu Thr Tyr Ile Ser Arg Asp Leu
785                     790                     795                 800
Gln Phe Ile Ser Lys Val Ile Gln Ser Glu Gly Val Met His Pro Thr
                805                     810                     815
Pro Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr Ile Leu
            820                     825                     830
Asp Asp Ile Lys Thr Ser Ala Glu Ser Ile Gly Ser Leu Cys Gln Glu
        835                     840                     845
Leu Glu Phe Arg Gly Glu Ser Ile Ile Val Ser Leu Ile Leu Arg Asn
    850                     855                     860
Phe Trp Leu Tyr Asn Leu Tyr Met His Glu Ser Lys Gln His Pro Leu
865                     870                     875                 880
Ala Gly Lys Gln Leu Phe Lys Gln Leu Asn Lys Thr Leu Thr Ser Val
                885                     890                     895
Gln Arg Phe Phe Glu Ile Lys Lys Glu Asn Glu Val Val Asp Leu Trp
            900                     905                     910
Met Asn Ile Pro Met Gln Phe Gly Gly Gly Asp Pro Val Val Phe Tyr
        915                     920                     925
Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala Ile Ser
    930                     935                     940
His Val Asp Ile Leu Leu Lys Ile Ser Ala Asn Ile Lys Asn Glu Thr
945                     950                     955                 960
Lys Val Ser Phe Phe Lys Ala Leu Leu Ser Ile Glu Lys Asn Glu Arg
                965                     970                     975
Ala Thr Leu Thr Thr Leu Met Arg Asp Pro Gln Ala Val Gly Ser Glu
            980                     985                     990
Arg Gln Ala Lys Val Thr Ser Asp Ile Asn Arg Thr Ala Val Thr Ser
        995                     1000                    1005
Ile Leu Ser Leu Ser Pro Asn Gln Leu Phe Ser Asp Ser Ala Ile His
    1010                    1015                    1020
Tyr Ser Arg Asn Glu Glu Glu Val Gly Ile Ile Ala Glu Asn Ile Thr
1025                    1030                    1035                1040
Pro Val Tyr Pro His Gly Leu Arg Val Leu Tyr Glu Ser Leu Pro Phe
                1045                    1050                    1055
His Lys Ala Glu Lys Val Val Asn Met Ile Ser Gly Thr Lys Ser Ile
            1060                    1065                    1070
Thr Asn Leu Leu Gln Arg Thr Ser Ala Ile Asn Gly Glu Asp Ile Asp
        1075                    1080                    1085
Arg Ala Val Ser Met Met Leu Glu Asn Leu Gly Leu Leu Ser Arg Ile
    1090                    1095                    1100
Leu Ser Val Val Val Asp Ser Ile Glu Ile Pro Ile Lys Ser Asn Gly
1105                    1110                    1115                1120
Arg Leu Ile Cys Cys Gln Ile Ser Arg Thr Leu Arg Glu Thr Ser Trp
                1125                    1130                    1135
Asn Asn Met Glu Ile Val Gly Val Thr Ser Pro Ser Ile Thr Thr Cys
            1140                    1145                    1150
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Met Asp Val Ile Tyr Ala Thr Ser Ser His Leu Lys Gly Ile Ile Ile
1155 1160 1165

Glu Lys Phe Ser Thr Asp Arg Thr Thr Arg Gly Gln Arg Gly Pro Lys
1170 1175 1180

Ser Pro Trp Val Gly Ser Ser Thr Gln Glu Lys Lys Leu Val Pro Val
1185 1190 1195 1200

Tyr Asn Arg Gln Ile Leu Ser Lys Gln Gln Arg Glu Gln Leu Glu Ala
1205 1210 1215

Ile Gly Lys Met Arg Trp Val Tyr Lys Gly Thr Pro Gly Leu Arg Arg
1220 1225 1230

Leu Leu Asn Lys Ile Cys Leu Gly Ser Leu Gly Ile Ser Tyr Lys Cys
1235 1240 1245

Val Lys Pro Leu Leu Pro Arg Phe Met Ser Val Asn Phe Leu His Arg
1250 1255 1260

Leu Ser Val Ser Ser Arg Pro Met Glu Phe Pro Ala Ser Val Pro Ala
1265 1270 1275 1280

Tyr Arg Thr Thr Asn Tyr His Phe Asp Thr Ser Pro Ile Asn Gln Ala
1285 1290 1295

Leu Ser Glu Arg Phe Gly Asn Glu Asp Ile Asn Leu Val Phe Gln Asn
1300 1305 1310

Ala Ile Ser Cys Gly Ile Ser Ile Met Ser Val Val Glu Gln Leu Thr
1315 1320 1325

Gly Arg Ser Pro Lys Gln Leu Val Leu Ile Pro Gln Leu Glu Glu Ile
1330 1335 1340

Asp Ile Met Pro Pro Pro Val Phe Gln Gly Lys Phe Asn Tyr Lys Leu
1345 1350 1355 1360

Val Asp Lys Ile Thr Ser Asp Gln His Ile Phe Ser Pro Asp Lys Ile
1365 1370 1375

Asp Met Leu Thr Leu Gly Lys Met Leu Met Pro Thr Ile Lys Gly Gln
1380 1385 1390

Lys Thr Asp Gln Phe Leu Asn Lys Arg Glu Asn Tyr Phe His Gly Asn
1395 1400 1405

Asn Leu Ile Glu Ser Leu Ser Ala Ala Leu Ala Cys His Trp Cys Gly
1410 1415 1420

Ile Leu Thr Glu Gln Cys Ile Glu Asn Asn Ile Phe Lys Lys Asp Trp
1425 1430 1435 1440

Gly Asp Gly Phe Ile Ser Asp His Ala Phe Met Asp Phe Lys Ile Phe
1445 1450 1455

Leu Cys Val Phe Lys Thr Lys Leu Leu Cys Ser Trp Gly Ser Gln Gly
1460 1465 1470

Lys Asn Ile Lys Asp Glu Asp Ile Val Asp Glu Ser Ile Asp Lys Leu
1475 1480 1485

Leu Arg Ile Asp Asn Thr Phe Trp Arg Met Phe Ser Lys Val Met Phe
1490 1495 1500

Glu Pro Lys Val Lys Lys Arg Ile Met Leu Tyr Asp Val Lys Phe Leu
1505 1510 1515 1520

Ser Leu Val Gly Tyr Ile Gly Phe Lys Asn Trp Phe Ile Glu Gln Leu
1525 1530 1535

Arg Ser Ala Glu Leu His Glu Ile Pro Trp Ile Val Asn Ala Glu Gly
1540 1545 1550

Asp Leu Val Glu Ile Lys Ser Ile Lys Ile Tyr Leu Gln Leu Ile Glu
1555 1560 1565

Gln Ser Leu Phe Leu Arg Ile Thr Val Leu Asn Tyr Thr Asp Met Ala
1570 1575 1580

His Ala Leu Thr Arg Leu Ile Arg Lys Lys Leu Met Cys Asp Asn Ala
1585 1590 1595 1600

Leu Leu Thr Pro Ile Ser Ser Pro Met Val Asn Leu Thr Gln Val Ile
1605 1610 1615

Asp Pro Thr Thr Gln Leu Asp Tyr Phe Pro Lys Ile Thr Phe Glu Arg
1620 1625 1630

Leu Lys Asn Tyr Asp Thr Ser Ser Asn Tyr Ala Lys Gly Lys Leu Thr

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        1635                1640                1645
Arg Asn Tyr Met Ile Leu Leu Pro Trp Gln His Val Asn Arg Tyr Asn
    1650                1655                1660
Phe Val Phe Ser Ser Thr Gly Cys Lys Val Ser Leu Lys Thr Cys Ile
1665                1670                1675                1680
Gly Lys Leu Met Lys Asp Leu Asn Pro Lys Val Leu Tyr Phe Ile Gly
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Glu Gly Ala Gly Asn Trp Met Ala Arg Thr Ala Cys Glu Tyr Pro Asp
            1700                1705                1710
Ile Lys Phe Val Tyr Arg Ser Leu Lys Asp Asp Leu Asp His His Tyr
        1715                1720                1725
Pro Leu Glu Tyr Gln Arg Val Ile Gly Glu Leu Ser Arg Ile Ile Asp
    1730                1735                1740
Ser Gly Glu Gly Leu Ser Met Glu Thr Thr Asp Ala Thr Gln Lys Thr
1745                1750                1755                1760
His Trp Asp Leu Ile His Arg Val Ser Lys Asp Ala Leu Leu Ile Thr
                1765                1770                1775
Leu Cys Asp Ala Glu Phe Lys Asp Arg Asp Asp Phe Phe Lys Met Val
            1780                1785                1790
Ile Leu Trp Arg Lys His Val Leu Ser Cys Arg Ile Cys Thr Thr Tyr
        1795                1800                1805
Gly Thr Asp Leu Tyr Leu Phe Ala Lys Tyr His Ala Lys Asp Cys Asn
    1810                1815                1820
Val Lys Leu Pro Phe Phe Val Arg Ser Val Ala Thr Phe Ile Met Gln
1825                1830                1835                1840
Gly Ser Lys Leu Ser Gly Ser Glu Cys Tyr Ile Leu Leu Thr Leu Gly
                1845                1850                1855
His His Asn Ser Leu Pro Cys His Gly Glu Ile Gln Asn Ser Lys Met
            1860                1865                1870
Lys Ile Ala Val Cys Asn Asp Phe Tyr Ala Ala Lys Lys Leu Asp Asn
        1875                1880                1885
Lys Ser Ile Glu Ala Asn Cys Lys Ser Leu Leu Ser Gly Leu Arg Ile
    1890                1895                1900
Pro Ile Asn Lys Lys Glu Leu Asp Arg Gln Arg Arg Leu Leu Thr Leu
1905                1910                1915                1920
Gln Ser Asn His Ser Ser Val Ala Thr Val Gly Gly Ser Lys Ile Ile
                1925                1930                1935
Glu Ser Lys Trp Leu Thr Asn Lys Ala Ser Thr Ile Ile Asp Trp Leu
            1940                1945                1950
Glu His Ile Leu Asn Ser Pro Lys Gly Glu Leu Asn Tyr Asp Phe Phe
        1955                1960                1965
Glu Ala Leu Glu Asn Thr Tyr Pro Asn Met Ile Lys Leu Ile Asp Asn
    1970                1975                1980
Leu Gly Asn Ala Glu Ile Lys Lys Leu Ile Lys Val Thr Gly Tyr Met
1985                1990                1995                2000
Leu Val Ser Lys Lys
                2005
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<210> 332
<211> 2005
<212> PRT
<213> human metapneumo virus

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            20                  25                  30
Cys Leu Leu Lys Arg Pro Tyr Leu Lys Asn Asp Asn Thr Ala Lys Val
        35                  40                  45
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Ala Val Glu Asn Pro Val Val Glu His Val Arg Leu Arg Asn Ala Val
50 55 60
Met Thr Lys Met Lys Ile Ser Asp Tyr Lys Val Val Glu Pro Val Asn
65 70 75 80
Met Gln His Glu Ile Met Lys Asn Ile His Ser Cys Glu Leu Thr Leu
85 90 95
Leu Lys Gln Phe Leu Thr Arg Ser Lys Asn Ile Ser Ser Leu Lys Leu
100 105 110
Asn Met Ile Cys Asp Trp Leu Gln Leu Lys Ser Thr Ser Asp Asn Thr
115 120 125
Ser Ile Leu Asn Phe Ile Asp Val Glu Phe Ile Pro Val Trp Val Ser
130 135 140
Asn Trp Phe Ser Asn Trp Tyr Asn Leu Asn Lys Leu Ile Leu Glu Phe
145 150 155 160
Arg Arg Glu Glu Val Ile Arg Thr Gly Ser Ile Leu Cys Arg Ser Leu
165 170 175
Gly Lys Leu Val Phe Ile Val Ser Ser Tyr Gly Cys Val Val Lys Ser
180 185 190
Asn Lys Ser Lys Arg Val Ser Phe Phe Thr Tyr Asn Gln Leu Leu Thr
195 200 205
Trp Lys Asp Val Met Leu Ser Arg Phe Asn Ala Asn Phe Cys Ile Trp
210 215 220
Val Ser Asn Asn Leu Asn Lys Asn Gln Glu Gly Leu Gly Leu Arg Ser
225 230 235 240
Asn Leu Gln Gly Met Leu Thr Asn Lys Leu Tyr Glu Thr Val Asp Tyr
245 250 255
Met Leu Ser Leu Cys Cys Asn Glu Gly Phe Ser Leu Val Lys Glu Phe
260 265 270
Glu Gly Phe Ile Met Ser Glu Ile Leu Lys Ile Thr Glu His Ala Gln
275 280 285
Phe Ser Thr Arg Phe Arg Asn Thr Leu Leu Asn Gly Leu Thr Glu Gln
290 295 300
Leu Ser Val Leu Lys Ala Lys Asn Arg Ser Arg Val Leu Gly Thr Ile
305 310 315 320
Leu Glu Asn Asn Asn Tyr Pro Met Tyr Glu Val Val Leu Lys Leu Leu
325 330 335
Gly Asp Thr Leu Lys Ser Ile Lys Leu Leu Ile Asn Lys Asn Leu Glu
340 345 350
Asn Ala Ala Glu Leu Tyr Tyr Ile Phe Arg Ile Phe Gly His Pro Met
355 360 365
Val Asp Glu Arg Glu Ala Met Asp Ala Val Lys Leu Asn Asn Glu Ile
370 375 380
Thr Lys Ile Leu Lys Leu Glu Ser Leu Thr Glu Leu Arg Gly Ala Phe
385 390 395 400
Ile Leu Arg Ile Ile Lys Gly Phe Val Asp Asn Asn Lys Arg Trp Pro
405 410 415
Lys Ile Lys Asn Leu Lys Val Leu Ser Lys Arg Trp Ala Met Tyr Phe
420 425 430
Lys Ala Lys Ser Tyr Pro Ser Gln Leu Glu Leu Ser Val Gln Asp Phe
435 440 445
Leu Glu Leu Ala Ala Val Gln Phe Glu Gln Glu Phe Ser Val Pro Glu
450 455 460
Lys Thr Asn Leu Glu Met Val Leu Asn Asp Lys Ala Ile Ser Pro Pro
465 470 475 480
Lys Lys Leu Ile Trp Ser Val Tyr Pro Lys Asn Tyr Leu Pro Glu Thr
485 490 495
Ile Lys Asn Gln Tyr Leu Glu Glu Ala Phe Asn Ala Ser Asp Ser Gln
500 505 510
Arg Thr Arg Arg Val Leu Glu Phe Tyr Leu Lys Asp Cys Lys Phe Asp
515 520 525
Gln Lys Glu Leu Lys Arg Tyr Val Ile Lys Gln Glu Tyr Leu Asn Asp

530 535 540
Lys Asp His Ile Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser Val
545 550 555 560
Gly Arg Met Phe Ala Met Gln Pro Gly Lys Gln Arg Gln Ile Gln Ile
565 570 575
Leu Ala Glu Lys Leu Leu Ala Asp Asn Ile Val Pro Phe Phe Pro Glu
580 585 590
Thr Leu Thr Lys Tyr Gly Asp Leu Asp Leu Gln Arg Ile Met Glu Ile
595 600 605
Lys Ser Glu Leu Ser Ser Ile Lys Thr Arg Lys Asn Asp Ser Tyr Asn
610 615 620
Asn Tyr Ile Ala Arg Ala Ser Ile Val Thr Asp Leu Ser Lys Phe Asn
625 630 635 640
Gln Ala Phe Arg Tyr Glu Thr Thr Ala Ile Cys Ala Asp Val Ala Asp
645 650 655
Glu Leu His Gly Thr Gln Ser Leu Phe Cys Trp Leu His Leu Ile Val
660 665 670
Pro Met Thr Thr Met Ile Cys Ala Tyr Arg His Ala Pro Pro Glu Thr
675 680 685
Lys Gly Glu Tyr Asp Ile Asp Lys Ile Gln Glu Gln Ser Gly Leu Tyr
690 695 700
Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu Trp Thr
705 710 715 720
Met Glu Ala Ile Ser Leu Leu Asp Val Val Ser Val Lys Thr Arg Cys
725 730 735
Gln Met Thr Ser Leu Leu Asn Gly Asp Asn Gln Ser Ile Asp Val Ser
740 745 750
Lys Pro Val Lys Leu Ser Glu Gly Ile Asp Glu Val Lys Ala Asp Tyr
755 760 765
Ser Leu Ala Ile Arg Met Leu Lys Glu Ile Arg Asp Ala Tyr Lys Asn
770 775 780
Ile Gly His Lys Leu Lys Glu Gly Glu Thr Tyr Ile Ser Arg Asp Leu
785 790 795 800
Gln Phe Ile Ser Lys Val Ile Gln Ser Glu Gly Val Met His Pro Thr
805 810 815
Pro Ile Lys Lys Ile Leu Arg Val Gly Pro Trp Ile Asn Thr Ile Leu
820 825 830
Asp Asp Ile Lys Thr Ser Ala Glu Ser Ile Gly Ser Leu Cys Gln Glu
835 840 845
Leu Glu Phe Arg Gly Glu Ser Ile Leu Val Ser Leu Ile Leu Arg Asn
850 855 860
Phe Trp Leu Tyr Asn Leu Tyr Met Tyr Glu Ser Lys Gln His Pro Leu
865 870 875 880
Ala Gly Lys Gln Leu Phe Lys Gln Leu Asn Lys Thr Leu Thr Ser Val
885 890 895
Gln Arg Phe Phe Glu Leu Lys Lys Glu Asn Asp Val Val Asp Leu Trp
900 905 910
Met Asn Ile Pro Met Gln Phe Gly Gly Gly Asp Pro Val Val Phe Tyr
915 920 925
Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala Ile Ser
930 935 940
His Val Asp Leu Leu Leu Lys Val Ser Asn Asn Ile Lys Asp Glu Thr
945 950 955 960
Lys Ile Arg Phe Phe Lys Ala Leu Leu Ser Ile Glu Lys Asn Glu Arg
965 970 975
Ala Thr Leu Thr Thr Leu Met Arg Asp Pro Gln Ala Val Gly Ser Glu
980 985 990
Arg Gln Ala Lys Val Thr Ser Asp Ile Asn Arg Thr Ala Val Thr Ser
995 1000 1005
Ile Leu Ser Leu Ser Pro Asn Gln Leu Phe Cys Asp Ser Ala Ile His
1010 1015 1020

Tyr Ser Arg Asn Glu Glu Glu Val Gly Ile Ile Ala Asp Asn Ile Thr
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Pro Val Tyr Pro His Gly Leu Arg Val Leu Tyr Glu Ser Leu Pro Phe
1045 1050 1055
His Lys Ala Glu Lys Val Val Asn Met Ile Ser Gly Thr Lys Ser Ile
1060 1065 1070
Thr Asn Leu Leu Gln Arg Thr Ser Ala Ile Asn Gly Glu Asp Ile Asp
1075 1080 1085
Arg Ala Val Ser Met Met Leu Glu Asn Leu Gly Leu Leu Ser Arg Ile
1090 1095 1100
Leu Ser Val Ile Ile Asn Ser Ile Glu Ile Pro Ile Lys Ser Asn Gly
1105 1110 1115 1120
Arg Leu Ile Cys Cys Gln Ile Ser Lys Thr Leu Arg Glu Lys Ser Trp
1125 1130 1135
Asn Asn Met Glu Ile Val Gly Val Thr Ser Pro Ser Ile Val Thr Cys
1140 1145 1150
Met Asp Val Val Tyr Ala Thr Ser Ser His Leu Lys Gly Ile Ile Ile
1155 1160 1165
Glu Lys Phe Ser Thr Asp Lys Thr Thr Arg Gly Gln Arg Gly Pro Lys
1170 1175 1180
Ser Pro Trp Val Gly Ser Ser Thr Gln Glu Lys Lys Leu Val Pro Val
1185 1190 1195 1200
Tyr Asn Arg Gln Ile Leu Ser Lys Gln Gln Lys Glu Gln Leu Glu Ala
1205 1210 1215
Ile Gly Lys Met Arg Trp Val Tyr Lys Gly Thr Pro Gly Leu Arg Arg
1220 1225 1230
Leu Leu Asn Lys Ile Cys Ile Gly Ser Leu Gly Ile Ser Tyr Lys Cys
1235 1240 1245
Val Lys Pro Leu Leu Pro Arg Phe Met Ser Val Asn Phe Leu His Arg
1250 1255 1260
Leu Ser Val Ser Ser Arg Pro Met Glu Phe Pro Ala Ser Val Pro Ala
1265 1270 1275 1280
Tyr Arg Thr Thr Asn Tyr His Phe Asp Thr Ser Pro Ile Asn Gln Ala
1285 1290 1295
Leu Ser Glu Arg Phe Gly Asn Glu Asp Ile Asn Leu Val Phe Gln Asn
1300 1305 1310
Ala Ile Ser Cys Gly Ile Ser Ile Met Ser Val Val Glu Gln Leu Thr
1315 1320 1325
Gly Arg Ser Pro Lys Gln Leu Val Leu Ile Pro Gln Leu Glu Glu Ile
1330 1335 1340
Asp Ile Met Pro Pro Pro Val Phe Gln Gly Lys Phe Asn Tyr Lys Leu
1345 1350 1355 1360
Val Asp Lys Ile Thr Ser Asp Gln His Ile Phe Ser Pro Asp Lys Ile
1365 1370 1375
Asp Ile Leu Thr Leu Gly Lys Met Leu Met Pro Thr Ile Lys Gly Gln
1380 1385 1390
Lys Thr Asp Gln Phe Leu Asn Lys Arg Glu Asn Tyr Phe His Gly Asn
1395 1400 1405
Asn Leu Ile Glu Ser Leu Ser Ala Ala Leu Ala Cys His Trp Cys Gly
1410 1415 1420
Ile Leu Thr Glu Gln Cys Ile Glu Asn Asn Ile Phe Arg Lys Asp Trp
1425 1430 1435 1440
Gly Asp Gly Phe Ile Ser Asp His Ala Phe Met Asp Phe Lys Val Phe
1445 1450 1455
Leu Cys Val Phe Lys Thr Lys Leu Leu Cys Ser Trp Gly Ser Gln Gly
1460 1465 1470
Lys Asn Val Lys Asp Glu Asp Ile Ile Asp Glu Ser Ile Asp Lys Leu
1475 1480 1485
Leu Arg Ile Asp Asn Thr Phe Trp Arg Met Phe Ser Lys Val Met Phe
1490 1495 1500
Glu Ser Lys Val Lys Lys Arg Ile Met Leu Tyr Asp Val Lys Phe Leu

1505 1510 1515 1520
Ser Leu Val Gly Tyr Ile Gly Phe Lys Asn Trp Phe Ile Glu Gln Leu
1525 1530 1535
Arg Val Val Glu Leu His Glu Val Pro Trp Ile Val Asn Ala Glu Gly
1540 1545 1550
Glu Leu Val Glu Ile Lys Ser Ile Lys Ile Tyr Leu Gln Leu Ile Glu
1555 1560 1565
Gln Ser Leu Ser Leu Arg Ile Thr Val Leu Asn Tyr Thr Asp Met Ala
1570 1575 1580
His Ala Leu Thr Arg Leu Ile Arg Lys Lys Leu Met Cys Asp Asn Ala
1585 1590 1595 1600
Leu Phe Asn Pro Ser Ser Ser Pro Met Phe Asn Leu Thr Gln Val Ile
1605 1610 1615
Asp Pro Thr Thr Gln Leu Asp Tyr Phe Pro Arg Ile Ile Phe Glu Arg
1620 1625 1630
Leu Lys Ser Tyr Asp Thr Ser Ser Asp Tyr Asn Lys Gly Lys Leu Thr
1635 1640 1645
Arg Asn Tyr Met Thr Leu Leu Pro Trp Gln His Val Asn Arg Tyr Asn
1650 1655 1660
Phe Val Phe Ser Ser Thr Gly Cys Lys Val Ser Leu Lys Thr Cys Ile
1665 1670 1675 1680
Gly Lys Leu Ile Lys Asp Leu Asn Pro Lys Val Leu Tyr Phe Ile Gly
1685 1690 1695
Glu Gly Ala Gly Asn Trp Met Ala Arg Thr Ala Cys Glu Tyr Pro Asp
1700 1705 1710
Ile Lys Phe Val Tyr Arg Ser Leu Lys Asp Asp Leu Asp His His Tyr
1715 1720 1725
Pro Leu Glu Tyr Gln Arg Val Ile Gly Asp Leu Asn Arg Val Ile Asp
1730 1735 1740
Ser Gly Glu Gly Leu Ser Met Glu Thr Thr Asp Ala Thr Gln Lys Thr
1745 1750 1755 1760
His Trp Asp Leu Ile His Arg Ile Ser Lys Asp Ala Leu Leu Ile Thr
1765 1770 1775
Leu Cys Asp Ala Glu Phe Lys Asn Arg Asp Asp Phe Phe Lys Met Val
1780 1785 1790
Ile Leu Trp Arg Lys His Val Leu Ser Cys Arg Ile Cys Thr Ala Tyr
1795 1800 1805
Gly Thr Asp Leu Tyr Leu Phe Ala Lys Tyr His Ala Val Asp Cys Asn
1810 1815 1820
Ile Lys Leu Pro Phe Phe Val Arg Ser Val Ala Thr Phe Ile Met Gln
1825 1830 1835 1840
Gly Ser Lys Leu Ser Gly Ser Glu Cys Tyr Ile Leu Leu Thr Leu Gly
1845 1850 1855
His His Asn Asn Leu Pro Cys His Gly Glu Ile Gln Asn Ser Lys Met
1860 1865 1870
Arg Ile Ala Val Cys Asn Asp Phe Tyr Ala Ser Lys Lys Leu Asp Asn
1875 1880 1885
Lys Ser Ile Glu Ala Asn Cys Lys Ser Leu Leu Ser Gly Leu Arg Ile
1890 1895 1900
Pro Ile Asn Lys Lys Glu Leu Asn Arg Gln Lys Lys Leu Leu Thr Leu
1905 1910 1915 1920
Gln Ser Asn His Ser Ser Ile Ala Thr Val Gly Gly Ser Lys Ile Ile
1925 1930 1935
Glu Ser Lys Trp Leu Lys Asn Lys Ala Ser Thr Ile Ile Asp Trp Leu
1940 1945 1950
Glu His Ile Leu Asn Ser Pro Lys Gly Glu Leu Asn Tyr Asp Phe Phe
1955 1960 1965
Glu Ala Leu Glu Asn Thr Tyr Pro Asn Met Ile Lys Leu Ile Asp Asn
1970 1975 1980
Leu Gly Asn Ala Glu Ile Lys Lys Leu Ile Lys Val Thr Gly Tyr Met
1985 1990 1995 2000

Leu Val Ser Lys Lys
2005

<210> 333
<211> 2005
<212> PRT
<213> human metapneumo virus

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Cys Leu Leu Lys Arg Pro Tyr Leu Lys Lys Asp Asn Thr Ala Lys Val
35 40 45
Ala Val Glu Asn Pro Val Val Glu His Val Arg Leu Arg Asn Ala Val
50 55 60
Met Thr Lys Met Lys Ile Ser Asp Tyr Lys Val Val Glu Pro Ile Asn
65 70 75 80
Met Gln His Glu Ile Met Lys Asn Ile His Ser Cys Glu Leu Thr Leu
85 90 95
Leu Lys Gln Phe Leu Thr Arg Ser Lys Asn Ile Ser Ser Leu Lys Leu
100 105 110
Ser Met Ile Cys Asp Trp Leu Gln Leu Lys Ser Thr Ser Asp Asn Thr
115 120 125
Ser Ile Leu Asn Phe Ile Asp Val Glu Phe Ile Pro Val Trp Val Ser
130 135 140
Asn Trp Phe Ser Asn Trp Tyr Asn Leu Asn Lys Leu Ile Leu Glu Phe
145 150 155 160
Arg Arg Glu Glu Val Ile Arg Thr Gly Ser Ile Leu Cys Arg Ser Leu
165 170 175
Gly Lys Leu Val Phe Ile Val Ser Ser Tyr Gly Cys Val Val Lys Ser
180 185 190
Asn Lys Ser Lys Arg Val Ser Phe Phe Thr Tyr Asn Gln Leu Leu Thr
195 200 205
Trp Lys Asp Val Met Leu Ser Arg Phe Asn Ala Asn Phe Cys Ile Trp
210 215 220
Val Ser Asn Asn Leu Asn Lys Asn Gln Glu Gly Leu Gly Phe Arg Ser
225 230 235 240
Asn Leu Gln Gly Met Leu Thr Asn Lys Leu Tyr Glu Thr Val Asp Tyr
245 250 255
Met Leu Ser Leu Cys Ser Asn Glu Gly Phe Ser Leu Val Lys Glu Phe
260 265 270
Glu Gly Phe Ile Met Ser Glu Ile Leu Lys Ile Thr Glu His Ala Gln
275 280 285
Phe Ser Thr Arg Phe Arg Asn Thr Leu Leu Asn Gly Leu Thr Glu Gln
290 295 300
Leu Ser Met Leu Lys Ala Lys Asn Arg Ser Arg Val Leu Gly Thr Ile
305 310 315 320
Leu Glu Asn Asn Asp Tyr Pro Met Tyr Glu Val Val Leu Lys Leu Leu
325 330 335
Gly Asp Thr Leu Lys Ser Ile Lys Leu Leu Ile Asn Lys Asn Leu Glu
340 345 350
Asn Ala Ala Glu Leu Tyr Tyr Ile Phe Arg Ile Phe Gly His Pro Met
355 360 365
Val Asp Glu Arg Glu Ala Met Asp Ala Val Lys Leu Asn Asn Glu Ile
370 375 380
Thr Lys Ile Leu Lys Leu Glu Ser Leu Thr Glu Leu Arg Gly Ala Phe
385 390 395 400
Ile Leu Arg Ile Ile Lys Gly Phe Val Asp Asn Asn Lys Arg Trp Pro

405 410 415
Lys Ile Lys Asn Leu Lys Val Leu Ser Lys Arg Trp Val Met Tyr Phe
420 425 430
Lys Ala Lys Ser Tyr Pro Ser Gln Leu Glu Leu Ser Val Gln Asp Phe
435 440 445
Leu Glu Leu Ala Ala Val Gln Phe Glu Gln Glu Phe Ser Val Pro Glu
450 455 460
Lys Thr Asn Leu Glu Met Val Leu Asn Asp Lys Ala Ile Ser Pro Pro
465 470 475 480
Lys Lys Leu Ile Trp Ser Val Tyr Pro Lys Asn Tyr Leu Pro Glu Ile
485 490 495
Ile Lys Asn Gln Tyr Leu Glu Glu Val Phe Asn Ala Ser Asp Ser Gln
500 505 510
Arg Thr Arg Arg Val Leu Glu Phe Tyr Leu Lys Asp Cys Lys Phe Asp
515 520 525
Gln Lys Asp Leu Lys Arg Tyr Val Leu Lys Gln Glu Tyr Leu Asn Asp
530 535 540
Lys Asp His Ile Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser Val
545 550 555 560
Gly Arg Met Phe Ala Met Gln Pro Gly Lys Gln Arg Gln Ile Gln Ile
565 570 575
Leu Ala Glu Lys Leu Leu Ala Asp Asn Ile Val Pro Phe Phe Pro Glu
580 585 590
Thr Leu Thr Lys Tyr Gly Asp Leu Asp Leu Gln Arg Ile Met Glu Met
595 600 605
Lys Ser Glu Leu Ser Ser Ile Lys Thr Arg Lys Asn Asp Ser Tyr Asn
610 615 620
Asn Tyr Ile Ala Arg Ala Ser Ile Val Thr Asp Leu Ser Lys Phe Asn
625 630 635 640
Gln Ala Phe Arg Tyr Glu Thr Thr Ala Ile Cys Ala Asp Val Ala Asp
645 650 655
Glu Leu His Gly Thr Gln Ser Leu Phe Cys Trp Leu His Leu Ile Val
660 665 670
Pro Met Thr Thr Met Ile Cys Ala Tyr Arg His Ala Pro Pro Glu Thr
675 680 685
Lys Gly Glu Tyr Asp Ile Asp Lys Ile Glu Glu Gln Ser Gly Leu Tyr
690 695 700
Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu Trp Thr
705 710 715 720
Met Glu Ala Ile Ser Leu Leu Asp Val Val Ser Val Lys Thr Arg Cys
725 730 735
Gln Met Thr Ser Leu Leu Asn Gly Asp Asn Gln Ser Ile Asp Val Ser
740 745 750
Lys Pro Val Lys Leu Ser Glu Gly Ile Asp Glu Val Lys Ala Asp Tyr
755 760 765
Ser Leu Ala Ile Lys Met Leu Lys Glu Ile Arg Asp Ala Tyr Lys Asn
770 775 780
Ile Gly His Lys Leu Lys Glu Gly Glu Thr Tyr Ile Ser Arg Asp Leu
785 790 795 800
Gln Phe Ile Ser Lys Val Ile Gln Ser Glu Gly Val Met His Pro Thr
805 810 815
Pro Ile Lys Lys Ile Leu Arg Val Gly Pro Trp Ile Asn Thr Ile Leu
820 825 830
Asp Asp Ile Lys Thr Ser Ala Glu Ser Ile Gly Ser Leu Cys Gln Glu
835 840 845
Leu Glu Phe Arg Gly Glu Ser Met Leu Val Ser Leu Ile Leu Arg Asn
850 855 860
Phe Trp Leu Tyr Asn Leu Tyr Met His Glu Ser Lys Gln His Pro Leu
865 870 875 880
Ala Gly Lys Gln Leu Phe Lys Gln Leu Asn Lys Thr Leu Thr Ser Val
885 890 895

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Gln Arg Phe Phe Glu Leu Lys Lys Glu Asn Asp Val Val Asp Leu Trp
            900                 905                 910
Met Asn Ile Pro Met Gln Phe Gly Gly Gly Asp Pro Val Val Phe Tyr
        915                 920                 925
Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala Ile Ser
    930                 935                 940
His Val Asp Leu Leu Leu Lys Val Ser Asn Asn Ile Lys Asn Glu Thr
945                 950                 955                 960
Lys Ile Arg Phe Phe Lys Ala Leu Leu Ser Ile Glu Lys Asn Glu Arg
                965                 970                 975
Ala Thr Leu Thr Thr Leu Met Arg Asp Pro Gln Ala Val Gly Ser Glu
            980                 985                 990
Arg Gln Ala Lys Val Thr Ser Asp Ile Asn Arg Thr Ala Val Thr Ser
        995                 1000                1005
Ile Leu Ser Leu Ser Pro Asn Gln Leu Phe Cys Asp Ser Ala Ile His
    1010                1015                1020
Tyr Ser Arg Asn Glu Glu Glu Val Gly Ile Ile Ala Asp Asn Ile Thr
1025                1030                1035                1040
Pro Val Tyr Pro His Gly Leu Arg Val Leu Tyr Glu Ser Leu Pro Phe
                1045                1050                1055
His Lys Ala Glu Lys Val Val Asn Met Ile Ser Gly Thr Lys Ser Ile
            1060                1065                1070
Thr Asn Leu Leu Gln Arg Thr Ser Ala Ile Asn Gly Glu Asp Ile Asp
        1075                1080                1085
Arg Ala Val Ser Met Met Leu Glu Asn Leu Gly Leu Leu Ser Arg Ile
    1090                1095                1100
Leu Ser Val Ile Ile Asn Ser Ile Glu Ile Pro Ile Lys Ser Asn Gly
1105                1110                1115                1120
Arg Leu Ile Cys Cys Gln Ile Ser Lys Thr Leu Arg Glu Lys Ser Trp
                1125                1130                1135
Asn Asn Met Glu Ile Val Gly Val Thr Ser Pro Ser Ile Val Thr Cys
            1140                1145                1150
Met Asp Val Val Tyr Ala Thr Ser Ser His Leu Lys Gly Ile Ile Ile
        1155                1160                1165
Glu Lys Phe Ser Thr Asp Lys Thr Thr Arg Gly Gln Arg Gly Pro Lys
    1170                1175                1180
Ser Pro Trp Val Gly Ser Ser Thr Gln Glu Lys Lys Leu Val Pro Val
1185                1190                1195                1200
Tyr Asn Arg Gln Ile Leu Ser Lys Gln Gln Lys Glu Gln Leu Glu Ala
                1205                1210                1215
Ile Gly Lys Met Arg Trp Val Tyr Lys Gly Thr Pro Gly Leu Arg Arg
            1220                1225                1230
Leu Leu Asn Lys Ile Cys Ile Gly Ser Leu Gly Ile Ser Tyr Lys Cys
        1235                1240                1245
Val Lys Pro Leu Leu Pro Arg Phe Met Ser Val Asn Phe Leu His Arg
    1250                1255                1260
Leu Ser Val Ser Ser Arg Pro Met Glu Phe Pro Ala Ser Val Pro Ala
1265                1270                1275                1280
Tyr Arg Thr Thr Asn Tyr His Phe Asp Thr Ser Pro Ile Asn Gln Ala
                1285                1290                1295
Leu Ser Glu Arg Phe Gly Asn Glu Asp Ile Asn Leu Val Phe Gln Asn
            1300                1305                1310
Ala Ile Ser Cys Gly Ile Ser Ile Met Ser Val Val Glu Gln Leu Thr
        1315                1320                1325
Gly Arg Ser Pro Lys Gln Leu Val Leu Ile Pro Gln Leu Glu Glu Ile
    1330                1335                1340
Asp Ile Met Pro Pro Pro Val Phe Gln Gly Lys Phe Asn Tyr Lys Leu
1345                1350                1355                1360
Val Asp Lys Ile Thr Ser Asp Gln His Ile Phe Ser Pro Asp Lys Ile
                1365                1370                1375
Asp Ile Leu Thr Leu Gly Lys Met Leu Met Pro Thr Ile Lys Gly Gln
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1380 1385 1390
Lys Thr Asp Gln Phe Leu Asn Lys Arg Glu Asn Tyr Phe His Gly Asn
1395 1400 1405
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1410 1415 1420
Ile Leu Thr Glu Gln Cys Val Glu Asn Asn Ile Phe Arg Lys Asp Trp
1425 1430 1435 1440
Gly Asp Gly Phe Ile Ser Asp His Ala Phe Met Asp Phe Lys Ile Phe
1445 1450 1455
Leu Cys Val Phe Lys Thr Lys Leu Leu Cys Ser Trp Gly Ser Gln Gly
1460 1465 1470
Lys Asn Val Lys Asp Glu Asp Ile Ile Asp Glu Ser Ile Asp Lys Leu
1475 1480 1485
Leu Arg Ile Asp Asn Thr Phe Trp Arg Met Phe Ser Lys Val Met Phe
1490 1495 1500
Glu Ser Lys Val Lys Lys Arg Ile Met Leu Tyr Asp Val Lys Phe Leu
1505 1510 1515 1520
Ser Leu Val Gly Tyr Ile Gly Phe Lys Asn Trp Phe Ile Glu Gln Leu
1525 1530 1535
Arg Val Val Glu Leu His Glu Val Pro Trp Ile Val Asn Ala Glu Gly
1540 1545 1550
Glu Leu Val Glu Ile Lys Pro Ile Lys Ile Tyr Leu Gln Leu Ile Glu
1555 1560 1565
Gln Ser Leu Ser Leu Arg Ile Thr Val Leu Asn Tyr Thr Asp Met Ala
1570 1575 1580
His Ala Leu Thr Arg Leu Ile Arg Lys Lys Leu Met Cys Asp Asn Ala
1585 1590 1595 1600
Leu Phe Asn Pro Ser Ser Ser Pro Met Phe Ser Leu Thr Gln Val Ile
1605 1610 1615
Asp Pro Thr Thr Gln Leu Asp Tyr Phe Pro Lys Val Ile Phe Glu Arg
1620 1625 1630
Leu Lys Ser Tyr Asp Thr Ser Ser Asp Tyr Asn Lys Gly Lys Leu Thr
1635 1640 1645
Arg Asn Tyr Met Thr Leu Leu Pro Trp Gln His Val Asn Arg Tyr Asn
1650 1655 1660
Phe Val Phe Ser Ser Thr Gly Cys Lys Ile Ser Leu Lys Thr Cys Ile
1665 1670 1675 1680
Gly Lys Leu Ile Lys Asp Leu Asn Pro Lys Val Leu Tyr Phe Ile Gly
1685 1690 1695
Glu Gly Ala Gly Asn Trp Met Ala Arg Thr Ala Cys Glu Tyr Pro Asp
1700 1705 1710
Ile Lys Phe Val Tyr Arg Ser Leu Lys Asp Asp Leu Asp His His Tyr
1715 1720 1725
Pro Leu Glu Tyr Gln Arg Val Ile Gly Asp Leu Asn Arg Val Ile Asp
1730 1735 1740
Gly Gly Glu Gly Leu Ser Met Glu Thr Thr Asp Ala Thr Gln Lys Thr
1745 1750 1755 1760
His Trp Asp Leu Ile His Arg Ile Ser Lys Asp Ala Leu Leu Ile Thr
1765 1770 1775
Leu Cys Asp Ala Glu Phe Lys Asn Arg Asp Asp Phe Phe Lys Met Val
1780 1785 1790
Ile Leu Trp Arg Lys His Val Leu Ser Cys Arg Ile Cys Thr Ala Tyr
1795 1800 1805
Gly Thr Asp Leu Tyr Leu Phe Ala Lys Tyr His Ala Thr Asp Cys Asn
1810 1815 1820
Ile Lys Leu Pro Phe Phe Val Arg Ser Val Ala Thr Phe Ile Met Gln
1825 1830 1835 1840
Gly Ser Lys Leu Ser Gly Ser Glu Cys Tyr Ile Leu Leu Thr Leu Gly
1845 1850 1855
His His Asn Asn Leu Pro Cys His Gly Glu Ile Gln Asn Ser Lys Met
1860 1865 1870

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Arg Ile Ala Val Cys Asn Asp Phe His Ala Ser Lys Lys Leu Asp Asn
        1875                1880                1885
Lys Ser Ile Glu Ala Asn Cys Lys Ser Leu Leu Ser Gly Leu Arg Ile
    1890                1895                1900
Pro Ile Asn Lys Lys Glu Leu Asn Arg Gln Lys Lys Leu Leu Thr Leu
1905                1910                1915                1920
Gln Ser Asn His Ser Ser Ile Ala Thr Val Gly Gly Ser Lys Ile Ile
                1925                1930                1935
Glu Ser Lys Trp Leu Lys Asn Lys Ala Ser Thr Ile Ile Asp Trp Leu
            1940                1945                1950
Glu His Ile Leu Asn Ser Pro Lys Gly Glu Leu Asn Tyr Asp Phe Phe
        1955                1960                1965
Glu Ala Leu Glu Asn Thr Tyr Pro Asn Met Ile Lys Leu Ile Asp Asn
    1970                1975                1980
Leu Gly Asn Ala Glu Ile Lys Lys Leu Ile Lys Val Pro Gly Tyr Met
1985                1990                1995                2000
Leu Val Ser Lys Lys
                2005
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<211> 6018
<212> DNA
<213> human metapneumo virus

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<212> PRT
<213> human metapneumo virus

<400> 338

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        35                  40                  45
Asn Thr Asp Arg Ala Asp Gly Leu Ser Ile Ile Ser Gly Ala Gly Arg
    50                  55                  60
Glu Asp Arg Thr Gln Asp Phe Val Leu Gly Ser Thr Asn Val Val Gln
65                  70                  75                  80
Gly Tyr Ile Asp Asp Asn Gln Ser Ile Thr Lys Ala Ala Ala Cys Tyr
                85                  90                  95
Ser Leu His Asn Ile Ile Lys Gln Leu Gln Glu Val Glu Val Arg Gln
            100                 105                 110
Ala Arg Asp Asn Lys Leu Ser Asp Ser Lys His Val Ala Leu His Asn
        115                 120                 125
Leu Val Leu Ser Tyr Met Glu Met Ser Lys Thr Pro Ala Ser Leu Ile
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Asn Asn Leu Lys Arg Leu Pro Arg Glu Lys Leu Lys Lys Leu Ala Lys
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<210> 339
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<213> human metapneumo virus

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35 40 45
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50 55 60
Glu Asp Arg Thr Gln Asp Phe Val Leu Gly Ser Thr Asn Val Val Gln
65 70 75 80
Gly Tyr Ile Asp Asp Asn Gln Ser Ile Thr Lys Ala Ala Ala Cys Tyr
85 90 95
Ser Leu His Asn Ile Ile Lys Gln Leu Gln Glu Val Glu Val Arg Gln
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Ala Arg Asp Ser Lys Leu Ser Asp Ser Lys His Val Ala Leu His Asn
115 120 125
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130 135 140
Asn Asn Leu Lys Arg Leu Pro Arg Glu Lys Leu Lys Lys Leu Ala Lys
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<211> 187
<212> PRT
<213> human metapneumo virus

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Arg Tyr Leu Leu Leu Arg Ser Asn Tyr Leu Leu Asn Gln Leu Leu Arg
35 40 45
Asn Thr Asp Lys Ala Asp Gly Leu Ser Ile Ile Ser Gly Ala Gly Arg
50 55 60
Glu Asp Arg Thr Gln Asp Phe Val Leu Gly Ser Thr Asn Val Val Gln
65 70 75 80
Gly Tyr Ile Asp Asp Asn Gln Gly Ile Thr Lys Ala Ala Ala Cys Tyr
85 90 95
Ser Leu His Asn Ile Ile Lys Gln Leu Gln Glu Thr Glu Val Arg Gln
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Ala Arg Asp Asn Lys Leu Ser Asp Ser Lys His Val Ala Leu His Asn
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Asn Asn Leu Lys Lys Leu Pro Arg Glu Lys Leu Lys Lys Leu Ala Arg

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        35                  40                  45
Asn Thr Asp Lys Ala Asp Gly Leu Ser Ile Ile Ser Gly Ala Gly Arg
    50                  55                  60
Glu Asp Arg Thr Gln Asp Phe Val Leu Gly Ser Thr Asn Val Val Gln
65                  70                  75                  80
Gly Tyr Ile Asp Asn Asn Gln Gly Ile Thr Lys Ala Ala Ala Cys Tyr
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Ser Leu His Asn Ile Ile Lys Gln Leu Gln Glu Ile Glu Val Arg Gln
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ggagcaggta gagaagatag aactcaagac tttgttcttg gttctactaa tgtggttcaa 240
gggtacattg atgacaacca aggaataacc aaggctgcag cttgctatag tctacacaac 300
ataatcaagc aactacaaga aacagaagta agacaggcta gagacaacaa gctttctgat 360
agcaaacatg tggcgctcca caacttgata ttatcctata tggagatgag caaaactcct 420
gcatctctaa tcaacaacct aaagaaacta ccaagggaaa aactgaagaa attagcaaga 480
ttaataattg atttatcagc aggaactgac aatgactctt catatgcctt gcaagacagt 540
gaaagcacta atcaagtgca gtaa 564

<210> 345
<211> 564
<212> DNA
<213> human metapneumo virus

<400> 345
atgtctcgca aagctccatg caaatatgaa gtacggggca agtgcaacag gggaagtgag 60
tgcaaattca accacaatta ctggagctgg cctgataggt atttattgtt aagatcaaat 120
tatctcttga atcagctttt aagaaacact gataaggctg atggtttgtc aataatatca 180
ggagcaggta gagaagatag gactcaagac tttgttcttg gttctactaa tgtggttcaa 240
gggtacattg ataacaatca aggaataaca aaggctgcag cttgctatag tctacataac 300
ataataaaac agctacaaga aatagaagta agacaggcta gagataataa gctttctgac 360
agcaaacatg tggcacttca caacttgata ttatcctata tggagatgag caaaactcct 420
gcatccctga ttaataacct aaagaaacta ccaagagaaa aactgaagaa attagcgaaa 480
ttaataattg atttatcagc aggaactgat aatgactctt catatgcctt gcaagacagt 540
gaaagcacta atcaagtgca gtaa 564

<210> 346
<211> 71
<212> PRT
<213> human metapneumo virus

<400> 346
Met Thr Leu His Met Pro Cys Lys Thr Val Lys Ala Leu Ile Lys Cys
1 5 10 15
Ser Glu His Gly Pro Val Phe Ile Thr Ile Glu Val Asp Asp Met Ile
20 25 30
Trp Thr His Lys Asp Leu Lys Glu Ala Leu Ser Asp Gly Ile Val Lys
35 40 45
Ser His Thr Asn Ile Tyr Asn Cys Tyr Leu Glu Asn Ile Glu Ile Ile
50 55 60
Tyr Val Lys Ala Tyr Leu Ser

65 70

<210> 347
<211> 71
<212> PRT
<213> human metapneumo virus

<400> 347
Met Thr Leu His Met Pro Cys Lys Thr Val Lys Ala Leu Ile Lys Cys
1 5 10 15
Ser Glu His Gly Pro Val Phe Ile Thr Ile Glu Val Asp Glu Met Ile
20 25 30
Trp Thr Gln Lys Glu Leu Lys Glu Ala Leu Ser Asp Gly Ile Val Lys
35 40 45
Ser His Thr Asn Ile Tyr Asn Cys Tyr Leu Glu Asn Ile Glu Ile Ile
50 55 60
Tyr Val Lys Ala Tyr Leu Ser
65 70

<210> 348
<211> 71
<212> PRT
<213> human metapneumo virus

<400> 348
Met Thr Leu His Met Pro Cys Lys Thr Val Lys Ala Leu Ile Lys Cys
1 5 10 15
Ser Lys His Gly Pro Lys Phe Ile Thr Ile Glu Ala Asp Asp Met Ile
20 25 30
Trp Thr His Lys Glu Leu Lys Glu Thr Leu Ser Asp Gly Ile Val Lys
35 40 45
Ser His Thr Asn Ile Tyr Ser Cys Tyr Leu Glu Asn Ile Glu Ile Ile
50 55 60
Tyr Val Lys Thr Tyr Leu Ser
65 70

<210> 349
<211> 71
<212> PRT
<213> human metapneumo virus

<400> 349
Met Thr Leu His Met Pro Cys Lys Thr Val Lys Ala Leu Ile Lys Cys
1 5 10 15
Ser Lys His Gly Pro Lys Phe Ile Thr Ile Glu Ala Asp Asp Met Ile
20 25 30
Trp Thr His Lys Glu Leu Lys Glu Thr Leu Ser Asp Gly Ile Val Lys
35 40 45
Ser His Thr Asn Ile Tyr Ser Cys Tyr Leu Glu Asn Ile Glu Ile Ile
50 55 60
Tyr Val Lys Ala Tyr Leu Ser
65 70

<210> 350
<211> 216
<212> DNA
<213> human metapneumo virus

<400> 350
atgactcttc atatgccttg caagacagtg aaagcactaa tcaagtgcag tgagcatggt 60
ccagttttca ttactataga ggttgatgac atgatatgga ctcacaagga cttaaaagaa 120
gctttatctg atgggatagt gaagtctcat actaacattt acaattgtta tttagaaaac 180
atagaaatta tatatgtcaa ggcttactta agttag 216

<210> 351
<211> 216
<212> DNA
<213> human metapneumo virus

<400> 351
atgactcttc atatgccctg caagacagtg aaagcactaa tcaagtgcag tgagcatggt 60
cctgttttca ttactataga ggttgatgaa atgatatgga ctcaaaaaga attaaaagaa 120
gctttgtccg atgggatagt gaagtctcac accaacattt acaattgtta tttagaaaac 180
atagaaatta tatatgtcaa ggcttactta agttag 216

<210> 352
<211> 216
<212> DNA
<213> human metapneumo virus

<400> 352
atgactcttc atatgccttg caagacagtg aaagcactaa tcaagtgcag taaacatggt 60
cccaaattca ttaccataga ggcagatgat atgatatgga ctcacaaaga attaaaagaa 120
acactgtctg atgggatagt aaaatcacac accaatattt atagttgtta cttagaaaat 180
atagaaataa tatatgttaa aacttactta agttag 216

<210> 353
<211> 216
<212> DNA
<213> human metapneumo virus

<400> 353
atgactcttc atatgccttg caagacagtg aaagcactaa tcaagtgcag taagcatggt 60
cccaaattca ttaccataga ggcagatgat atgatatgga cacacaaaga attaaaggag 120
acactgtctg atgggatagt aaaatcacac accaatattt acagttgtta tttagaaaat 180
atagaaataa tatatgttaa agcttactta agttag 216

<210> 354
<211> 727
<212> DNA
<213> human metapneumo virus

<400> 354
atgtctcgca aggctccgtg caaatatgaa gtgcggggca aatgcaatag aggaagtgag 60
tgcaagttta accacaatta ctggagttgg ccagatagat acttattaat aagatcaaat 120
tatttattaa atcaactttt aaggaacact gatagagctg atggcttatc aataatatca 180
ggagcaggca gagaagatag gacacaagat tttgtcctag gttccaccaa tgtggttcaa 240
ggttatattg atgataacca aagcataaca aaagctgcag cctgttacag tctacataat 300
ataatcaaac aactacaaga agttgaagtt aggcaggcta gagataacaa actatctgac 360
agcaaacatg tagcacttca caacttagtc ctatcttata tggagatgag caaaactcct 420
gcatctttaa tcaacaatct caagagactg ccgagagaga aactgaaaaa attagcaaag 480
ctcataattg acttatcagc aggtgctgaa aatgactctt catatgcctt gcaagacagt 540
gaaagcacta atcaagtgca gtgagcatgg tccagttttc attactatag aggttgatga 600
catgatatgg actcacaagg acttaaaaga agctttatct gatgggatag tgaagtctca 660
tactaacatt tacaattgtt atttagaaaa catagaaatt atatatgtca aggcttactt 720
aagttag 727

<210> 355

<211> 727
<212> DNA
<213> human metapneumo virus

<400> 355
atgtctcgca aggctccatg caaatatgaa gtgcggggca aatgcaacag aggaagtgag 60
tgtaagttta accacaatta ctggagttgg ccagatagat acttattaat aagatcaaac 120
tatctattaa atcagctttt aaggaacact gatagagctg atggcctatc aataatatca 180
ggcgcaggca gagaagacag aacgcaagat tttgttctag gttccaccaa tgtggttcaa 240
ggttatattg atgataacca aagcataaca aaagctgcag cctgctacag tctacacaac 300
ataatcaagc aactacaaga agttgaagtt aggcaggcta gagatagcaa actatctgac 360
agcaagcatg tggcactcca taacttaatc ttatcttaca tggagatgag caaaactccc 420
gcatctttaa tcaacaatct taaaagactg ccgagagaaa aactgaaaaa attagcaaag 480
ctgataattg acttatcagc aggcgctgac aatgactctt catatgccct gcaagacagt 540
gaaagcacta atcaagtgca gtgagcatgg tcctgttttc attactatag aggttgatga 600
aatgatatgg actcaaaaag aattaaaaga agctttgtcc gatgggatag tgaagtctca 660
caccaacatt tacaattgtt atttagaaaa catagaaatt atatatgtca aggcttactt 720
aagttag 727

<210> 356
<211> 727
<212> DNA
<213> human metapneumo virus

<400> 356
atgtctcgta aggctccatg caaatatgaa gtgcggggca aatgcaacag agggagtgat 60
tgcaaattca atcacaatta ctggagttgg cctgatagat atttattgtt aagatcaaat 120
tatctcttaa atcagctttt aagaaacaca gataaggctg atggtttgtc aataatatca 180
ggagcaggta gagaagatag aactcaagac tttgttcttg gttctactaa tgtggttcaa 240
gggtacattg atgacaacca aggaataacc aaggctgcag cttgctatag tctacacaac 300
ataatcaagc aactacaaga aacagaagta agacaggcta gagacaacaa gctttctgat 360
agcaaacatg tggcgctcca caacttgata ttatcctata tggagatgag caaaactcct 420
gcatctctaa tcaacaacct aaagaaacta ccaagggaaa aactgaagaa attagcaaga 480
ttaataattg atttatcagc aggaactgac aatgactctt catatgcctt gcaagacagt 540
gaaagcacta atcaagtgca gtaaacatgg tcccaaattc attaccatag aggcagatga 600
tatgatatgg actcacaaag aattaaaaga aacactgtct gatgggatag taaaatcaca 660
caccaatatt tatagttgtt acttagaaaa tatagaaata atatatgtta aaacttactt 720
aagttag 727

<210> 357
<211> 727
<212> DNA
<213> human metapneumo virus

<400> 357
atgtctcgca aagctccatg caaatatgaa gtacggggca agtgcaacag gggaagtgag 60
tgcaaattca accacaatta ctggagctgg cctgataggt atttattgtt aagatcaaat 120
tatctcttga atcagctttt aagaaacact gataaggctg atggtttgtc aataatatca 180
ggagcaggta gagaagatag gactcaagac tttgttcttg gttctactaa tgtggttcaa 240
gggtacattg ataacaatca aggaataaca aaggctgcag cttgctatag tctacataac 300
ataataaaac agctacaaga aatagaagta agacaggcta gagataataa gctttctgac 360
agcaaacatg tggcacttca caacttgata ttatcctata tggagatgag caaaactcct 420
gcatccctga ttaataacct aaagaaacta ccaagagaaa aactgaagaa attagcgaaa 480
ttaataattg atttatcagc aggaactgat aatgactctt catatgcctt gcaagacagt 540
gaaagcacta atcaagtgca gtaagcatgg tcccaaattc attaccatag aggcagatga 600
tatgatatgg acacacaaag aattaaagga gacactgtct gatgggatag taaaatcaca 660
caccaatatt tacagttgtt atttagaaaa tatagaaata atatatgtta aagcttactt 720
aagttag 727

<210> 358
<211> 254

<212> PRT
<213> human metapneumo virus

<400> 358
Met Glu Ser Tyr Leu Val Asp Thr Tyr Gln Gly Ile Pro Tyr Thr Ala
1   5   10   15
Ala Val Gln Val Asp Leu Ile Glu Lys Asp Leu Leu Pro Ala Ser Leu
            20   25   30
Thr Ile Trp Phe Pro Leu Phe Gln Ala Asn Thr Pro Pro Ala Val Leu
        35   40   45
Leu Asp Gln Leu Lys Thr Leu Thr Ile Thr Thr Leu Tyr Ala Ala Ser
    50   55   60
Gln Asn Gly Pro Ile Leu Lys Val Asn Ala Ser Ala Gln Gly Ala Ala
65   70   75   80
Met Ser Val Leu Pro Lys Lys Phe Glu Val Asn Ala Thr Val Ala Leu
                85   90   95
Asp Glu Tyr Ser Lys Leu Glu Phe Asp Lys Leu Thr Val Cys Glu Val
            100   105   110
Lys Thr Val Tyr Leu Thr Thr Met Lys Pro Tyr Gly Met Val Ser Lys
        115   120   125
Phe Val Ser Ser Ala Lys Ser Val Gly Lys Lys Thr His Asp Leu Ile
    130   135   140
Ala Leu Cys Asp Phe Met Asp Leu Glu Lys Asn Thr Pro Val Thr Ile
145   150   155   160
Pro Ala Phe Ile Lys Ser Val Ser Ile Lys Glu Ser Glu Ser Ala Thr
                165   170   175
Val Glu Ala Ala Ile Ser Ser Glu Ala Asp Gln Ala Leu Thr Gln Ala
            180   185   190
Lys Ile Ala Pro Tyr Ala Gly Leu Ile Met Ile Met Thr Met Asn Asn
        195   200   205
Pro Lys Gly Ile Phe Lys Lys Leu Gly Ala Gly Thr Gln Val Ile Val
    210   215   220
Glu Leu Gly Ala Tyr Val Gln Ala Glu Ser Ile Ser Lys Ile Cys Lys
225   230   235   240
Thr Trp Ser His Gln Gly Thr Arg Tyr Val Leu Lys Ser Arg
                245   250

<210> 359
<211> 254
<212> PRT
<213> human metapneumo virus

<400> 359
Met Glu Ser Tyr Leu Val Asp Thr Tyr Gln Gly Ile Pro Tyr Thr Ala
1   5   10   15
Ala Val Gln Val Asp Leu Val Glu Lys Asp Leu Leu Pro Ala Ser Leu
            20   25   30
Thr Ile Trp Phe Pro Leu Phe Gln Ala Asn Thr Pro Pro Ala Val Leu
        35   40   45
Leu Asp Gln Leu Lys Thr Leu Thr Ile Thr Thr Leu Tyr Ala Ala Ser
    50   55   60
Gln Ser Gly Pro Ile Leu Lys Val Asn Ala Ser Ala Gln Gly Ala Ala
65   70   75   80
Met Ser Val Leu Pro Lys Lys Phe Glu Val Asn Ala Thr Val Ala Leu
                85   90   95
Asp Glu Tyr Ser Lys Leu Glu Phe Asp Lys Leu Thr Val Cys Glu Val
            100   105   110
Lys Thr Val Tyr Leu Thr Thr Met Lys Pro Tyr Gly Met Val Ser Lys
        115   120   125
Phe Val Ser Ser Ala Lys Ser Val Gly Lys Lys Thr His Asp Leu Ile

130 135 140
Ala Leu Cys Asp Phe Met Asp Leu Glu Lys Asn Thr Pro Val Thr Ile
145 150 155 160
Pro Ala Phe Ile Lys Ser Val Ser Ile Lys Glu Ser Glu Ser Ala Thr
165 170 175
Val Glu Ala Ala Ile Ser Ser Glu Ala Asp Gln Ala Leu Thr Gln Ala
180 185 190
Lys Ile Ala Pro Tyr Ala Gly Leu Ile Met Ile Met Thr Met Asn Asn
195 200 205
Pro Lys Gly Ile Phe Lys Lys Leu Gly Ala Gly Thr Gln Val Ile Val
210 215 220
Glu Leu Gly Ala Tyr Val Gln Ala Glu Ser Ile Ser Lys Ile Cys Lys
225 230 235 240
Thr Trp Ser His Gln Gly Thr Arg Tyr Val Leu Lys Ser Ser
245 250

<210> 360
<211> 254
<212> PRT
<213> human metapneumo virus

<400> 360
Met Glu Ser Tyr Leu Val Asp Thr Tyr Gln Gly Ile Pro Tyr Thr Ala
1 5 10 15
Ala Val Gln Val Asp Leu Val Glu Lys Asp Leu Leu Pro Ala Ser Leu
20 25 30
Thr Ile Trp Phe Pro Leu Phe Gln Ala Asn Thr Pro Pro Ala Val Leu
35 40 45
Leu Asp Gln Leu Lys Thr Leu Thr Ile Thr Thr Leu Tyr Ala Ala Ser
50 55 60
Gln Asn Gly Pro Ile Leu Lys Val Asn Ala Ser Ala Gln Gly Ala Ala
65 70 75 80
Met Ser Val Leu Pro Lys Lys Phe Glu Val Asn Ala Thr Val Ala Leu
85 90 95
Asp Glu Tyr Ser Lys Leu Asp Phe Asp Lys Leu Thr Val Cys Asp Val
100 105 110
Lys Thr Val Tyr Leu Thr Thr Met Lys Pro Tyr Gly Met Val Ser Lys
115 120 125
Phe Val Ser Ser Ala Lys Ser Val Gly Lys Lys Thr His Asp Leu Ile
130 135 140
Ala Leu Cys Asp Phe Met Asp Leu Glu Lys Asn Ile Pro Val Thr Ile
145 150 155 160
Pro Ala Phe Ile Lys Ser Val Ser Ile Lys Glu Ser Glu Ser Ala Thr
165 170 175
Val Glu Ala Ala Ile Ser Ser Glu Ala Asp Gln Ala Leu Thr Gln Ala
180 185 190
Lys Ile Ala Pro Tyr Ala Gly Leu Ile Met Ile Met Thr Met Asn Asn
195 200 205
Pro Lys Gly Ile Phe Lys Lys Leu Gly Ala Gly Thr Gln Val Ile Val
210 215 220
Glu Leu Gly Ala Tyr Val Gln Ala Glu Ser Ile Ser Arg Ile Cys Lys
225 230 235 240
Ser Trp Ser His Gln Gly Thr Arg Tyr Val Leu Lys Ser Arg
245 250

<210> 361
<211> 254
<212> PRT
<213> human metapneumo virus

<400> 361

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Met Glu Ser Tyr Leu Val Asp Thr Tyr Gln Gly Ile Pro Tyr Thr Ala
1               5                   10                  15
Ala Val Gln Val Asp Leu Val Glu Lys Asp Leu Leu Pro Ala Ser Leu
            20                  25                  30
Thr Ile Trp Phe Pro Leu Phe Gln Ala Asn Thr Pro Pro Ala Val Leu
        35                  40                  45
Leu Asp Gln Leu Lys Thr Leu Thr Ile Thr Thr Leu Tyr Ala Ala Ser
    50                  55                  60
Gln Asn Gly Pro Ile Leu Lys Val Asn Ala Ser Ala Gln Gly Ala Ala
65                  70                  75                  80
Met Ser Val Leu Pro Lys Lys Phe Glu Val Asn Ala Thr Val Ala Leu
                85                  90                  95
Asp Glu Tyr Ser Lys Leu Asp Phe Asp Lys Leu Thr Val Cys Asp Val
            100                 105                 110
Lys Thr Val Tyr Leu Thr Thr Met Lys Pro Tyr Gly Met Val Ser Lys
        115                 120                 125
Phe Val Ser Ser Ala Lys Ser Val Gly Lys Lys Thr His Asp Leu Ile
    130                 135                 140
Ala Leu Cys Asp Phe Met Asp Leu Glu Lys Asn Ile Pro Val Thr Ile
145                 150                 155                 160
Pro Ala Phe Ile Lys Ser Val Ser Ile Lys Glu Ser Glu Ser Ala Thr
                165                 170                 175
Val Glu Ala Ala Ile Ser Ser Glu Ala Asp Gln Ala Leu Thr Gln Ala
            180                 185                 190
Lys Ile Ala Pro Tyr Ala Gly Leu Ile Met Ile Met Thr Met Asn Asn
        195                 200                 205
Pro Lys Gly Ile Phe Lys Lys Leu Gly Ala Gly Thr Gln Val Ile Val
    210                 215                 220
Glu Leu Gly Ala Tyr Val Gln Ala Glu Ser Ile Ser Arg Ile Cys Lys
225                 230                 235                 240
Ser Trp Ser His Gln Gly Thr Arg Tyr Val Leu Lys Ser Arg
                245                 250
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<210> 362
<211> 765
<212> DNA
<213> human metapneumo virus

<400> 362

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atggagtcct acctagtaga cacctatcaa ggcattcctt acacagcagc tgttcaagtt 60
gatctaatag aaaaggacct gttacctgca agcctaacaa tatggttccc tttgtttcag 120
gccaacacac caccagcagt gctgctcgat cagctaaaaa ccctgacaat aaccactctg 180
tatgctgcat cacaaaatgg tccaatactc aaagtgaatg catcagccca aggtgcagca 240
atgtctgtac ttcccaaaaa atttgaagtc aatgcgactg tagcactcga tgaatatagc 300
aaactggaat ttgacaaact cacagtctgt gaagtaaaaa cagtttactt aacaaccatg 360
aaaccatacg ggatggtatc aaaatttgtg agctcagcca aatcagttgg caaaaaaaca 420
catgatctaa tcgcactatg tgattttatg gatctagaaa agaacacacc tgttacaata 480
ccagcattca tcaaatcagt ttcaatcaaa gagagtgagt cagctactgt tgaagctgct 540
ataagcagtg aagcagacca agctctaaca caggccaaaa ttgcacctta tgcgggatta 600
attatgatca tgactatgaa caatcccaaa ggcatattca aaaagcttgg agctgggact 660
caagtcatag tagaactagg agcatatgtc caggctgaaa gcataagcaa aatatgcaag 720
acttggagcc atcaagggac aagatatgtc ttgaagtcca gataa                 765
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<210> 363
<211> 765
<212> DNA
<213> human metapneumo virus

<400> 363
atggagtcct atctggtaga cacttatcaa ggcatccctt acacagcagc tgttcaagtt 60
gatctagtag aaaaggacct gttacctgca agcctaacaa tatggttccc cttgtttcag 120
gccaatacac caccagcagt tctgcttgat cagctaaaga ctctgactat aactactctg 180
tatgctgcat cacaaagtgg tccaatacta aaagtgaatg catcagccca gggtgcagca 240
atgtctgtac ttcccaaaaa gtttgaagtc aatgcgactg tagcacttga cgaatatagc 300
aaattagaat ttgacaaact tacagtctgt gaagtaaaaa cagtttactt aacaaccatg 360
aaaccatatg ggatggtatc aaagtttgtg agctcggcca aatcagttgg caaaaaaaca 420
catgatctaa tcgcattatg tgattttatg gatctagaaa agaacacacc agttacaata 480
ccagcattta tcaaatcagt ttctatcaag gagagtgaat cagccactgt tgaagctgca 540
ataagcagtg aagcagacca agctctaaca caagccaaaa ttgcacctta tgcgggactg 600
atcatgatta tgaccatgaa caatcccaaa ggcatattca agaagcttgg agctgggacc 660
caagttatag tagaactagg agcatatgtc caggctgaaa gcataagtaa aatatgcaag 720
acttggagcc atcaaggaac aagatatgtg ctgaagtcca gttaa 765

<210> 364
<211> 765
<212> DNA
<213> human metapneumo virus

<400> 364
atggagtcct atctagtaga cacttatcaa ggcattccat atacagctgc tgttcaagtt 60
gacctggtag aaaaagattt actgccagca agtttgacaa tatggtttcc tttatttcag 120
gccaacacac caccagcagt tctgcttgat cagctaaaaa ccttgacaat aacaactctg 180
tatgctgcat cacagaatgg tccaatactc aaggtaaatg catctgccca aggtgctgcc 240
atgtctgtac ttcccaaaaa attcgaggta aatgcaactg tagcacttga tgaatacagt 300
aaacttgatt ttgacaagct gacggtctgc gatgttaaaa cagtttattt gacaactatg 360
aaaccgtacg ggatggtgtc aaaatttgtg agttcagcca aatcagttgg caaaaagaca 420
catgatctaa ttgcactatg tgacttcatg gacctagaga aaaatatacc tgtgacaata 480
ccagcattca taaagtcagt ttcaatcaaa gagagtgaat cagccactgt tgaagctgca 540
ataagcagcg aagccgacca agccttgaca caagccaaga ttgcgcccta tgcaggacta 600
attatgatca tgaccatgaa caatccaaaa ggtatattca agaaactagg ggctggaaca 660
caagtgatag tagagctggg ggcatatgtt caggctgaga gcatcagtag gatctgcaag 720
agctggagtc accaaggaac aagatacgta ctaaaatcca gataa 765

<210> 365
<211> 765
<212> DNA
<213> human metapneumo virus

<400> 365
atggagtcct atctagtgga cacttatcaa ggcattccct acacagctgc tgttcaagtt 60
gatctggtag aaaaagactt actaccagca agtttgacaa tatggtttcc tctattccaa 120
gccaacacac caccagcggt tttgctcgat cagctaaaaa ccttgactat aacaactctg 180
tatgctgcat cacagaatgg tccaatactc aaagtaaatg catcagctca gggtgctgct 240
atgtctgtac ttcccaaaaa attcgaagta aatgcaactg tggcacttga tgaatacagc 300
aaacttgact ttgacaagtt aacggtttgc gatgttaaaa cagtttattt gacaaccatg 360
aagccatatg ggatggtgtc aaaatttgtg agttcagcca aatcagttgg caaaaagaca 420
catgatctaa ttgcactgtg tgacttcatg gacctagaga aaaatatacc tgtgacaata 480
ccagcattca taaagtcagt ttcaatcaaa gagagtgagt cagccactgt tgaagctgca 540
ataagcagtg aggccgacca agcattaaca caagccaaaa ttgcacccta tgcaggacta 600
atcatgatca tgaccatgaa caatccaaaa ggtatattca agaaactagg agctggaaca 660
caagtgatag tagagctagg ggcatatgtt caagccgaga gcatcagcag gatctgcaag 720
agctggagtc accaaggaac aagatatgta ctaaaatcca gataa 765

<210> 366
<211> 394
<212> PRT
<213> human metapneumo virus

<400> 366

Met Ser Leu Gln Gly Ile His Leu Ser Asp Leu Ser Tyr Lys His Ala
1 5 10 15
Ile Leu Lys Glu Ser Gln Tyr Thr Ile Lys Arg Asp Val Gly Thr Thr
20 25 30
Thr Ala Val Thr Pro Ser Ser Leu Gln Gln Glu Ile Thr Leu Leu Cys
35 40 45
Gly Glu Ile Leu Tyr Ala Lys His Ala Asp Tyr Lys Tyr Ala Ala Glu
50 55 60
Ile Gly Ile Gln Tyr Ile Ser Thr Ala Leu Gly Ser Glu Arg Val Gln
65 70 75 80
Gln Ile Leu Arg Asn Ser Gly Ser Glu Val Gln Val Val Leu Thr Arg
85 90 95
Thr Tyr Ser Leu Gly Lys Ile Lys Asn Asn Lys Gly Glu Asp Leu Gln
100 105 110
Met Leu Asp Ile His Gly Val Glu Lys Ser Trp Val Glu Glu Ile Asp
115 120 125
Lys Glu Ala Arg Lys Thr Met Ala Thr Leu Leu Lys Glu Ser Ser Gly
130 135 140
Asn Ile Pro Gln Asn Gln Arg Pro Ser Ala Pro Asp Thr Pro Ile Ile
145 150 155 160
Leu Leu Cys Val Gly Ala Leu Ile Phe Thr Lys Leu Ala Ser Thr Ile
165 170 175
Glu Val Gly Leu Glu Thr Thr Val Arg Arg Ala Asn Arg Val Leu Ser
180 185 190
Asp Ala Leu Lys Arg Tyr Pro Arg Met Asp Ile Pro Lys Ile Ala Arg
195 200 205
Ser Phe Tyr Asp Leu Phe Glu Gln Lys Val Tyr His Arg Ser Leu Phe
210 215 220
Ile Glu Tyr Gly Lys Ala Leu Gly Ser Ser Ser Thr Gly Ser Lys Ala
225 230 235 240
Glu Ser Leu Phe Val Asn Ile Phe Met Gln Ala Tyr Gly Ala Gly Gln
245 250 255
Thr Met Leu Arg Trp Gly Val Ile Ala Arg Ser Ser Asn Asn Ile Met
260 265 270
Leu Gly His Val Ser Val Gln Ala Glu Leu Lys Gln Val Thr Glu Val
275 280 285
Tyr Asp Leu Val Arg Glu Met Gly Pro Glu Ser Gly Leu Leu His Leu
290 295 300
Arg Gln Ser Pro Lys Ala Gly Leu Leu Ser Leu Ala Asn Cys Pro Asn
305 310 315 320
Phe Ala Ser Val Val Leu Gly Asn Ala Ser Gly Leu Gly Ile Ile Gly
325 330 335
Met Tyr Arg Gly Arg Val Pro Asn Thr Glu Leu Phe Ser Ala Ala Glu
340 345 350
Ser Tyr Ala Lys Ser Leu Lys Glu Ser Asn Lys Ile Asn Phe Ser Ser
355 360 365
Leu Gly Leu Thr Asp Glu Glu Lys Glu Ala Ala Glu His Phe Leu Asn
370 375 380
Val Ser Asp Asp Ser Gln Asn Asp Tyr Glu
385 390

<210> 367
<211> 394
<212> PRT
<213> human metapneumo virus

<400> 367
Met Ser Leu Gln Gly Ile His Leu Ser Asp Leu Ser Tyr Lys His Ala
1 5 10 15
Ile Leu Lys Glu Ser Gln Tyr Thr Ile Lys Arg Asp Val Gly Thr Thr

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                20                  25                  30
Thr Ala Val Thr Pro Ser Ser Leu Gln Gln Glu Ile Thr Leu Leu Cys
        35                  40                  45
Gly Glu Ile Leu Tyr Ala Lys His Ala Asp Tyr Lys Tyr Ala Ala Glu
    50                  55                  60
Ile Gly Ile Gln Tyr Ile Ser Thr Ala Leu Gly Ser Glu Arg Val Gln
65                  70                  75                  80
Gln Ile Leu Arg Asn Ser Gly Ser Glu Val Gln Val Val Leu Thr Arg
                85                  90                  95
Thr Tyr Ser Leu Gly Lys Val Lys Asn Asn Lys Gly Glu Asp Leu Gln
            100                 105                 110
Met Leu Asp Ile His Gly Val Glu Lys Ser Trp Val Glu Glu Ile Asp
        115                 120                 125
Lys Glu Ala Arg Lys Thr Met Ala Thr Leu Leu Lys Glu Ser Ser Gly
    130                 135                 140
Asn Ile Pro Gln Asn Gln Arg Pro Ser Ala Pro Asp Thr Pro Ile Ile
145                 150                 155                 160
Leu Leu Cys Val Gly Ala Leu Ile Phe Thr Lys Leu Ala Ser Thr Ile
                165                 170                 175
Glu Val Gly Leu Glu Thr Thr Val Arg Arg Ala Asn Arg Val Leu Ser
            180                 185                 190
Asp Ala Leu Lys Arg Tyr Pro Arg Met Asp Ile Pro Lys Ile Ala Arg
        195                 200                 205
Ser Phe Tyr Asp Leu Phe Glu Gln Lys Val Tyr Tyr Arg Ser Leu Phe
    210                 215                 220
Ile Glu Tyr Gly Lys Ala Leu Gly Ser Ser Ser Thr Gly Ser Lys Ala
225                 230                 235                 240
Glu Ser Leu Phe Val Asn Ile Phe Met Gln Ala Tyr Gly Ala Gly Gln
                245                 250                 255
Thr Met Leu Arg Trp Gly Val Ile Ala Arg Ser Ser Asn Asn Ile Met
            260                 265                 270
Leu Gly His Val Ser Val Gln Ala Glu Leu Lys Gln Val Thr Glu Val
        275                 280                 285
Tyr Asp Leu Val Arg Glu Met Gly Pro Glu Ser Gly Leu Leu His Leu
    290                 295                 300
Arg Gln Ser Pro Lys Ala Gly Leu Leu Ser Leu Ala Asn Cys Pro Asn
305                 310                 315                 320
Phe Ala Ser Val Val Leu Gly Asn Ala Ser Gly Leu Gly Ile Ile Gly
                325                 330                 335
Met Tyr Arg Gly Arg Val Pro Asn Thr Glu Leu Phe Ser Ala Ala Glu
            340                 345                 350
Ser Tyr Ala Lys Ser Leu Lys Glu Ser Asn Lys Ile Asn Phe Ser Ser
        355                 360                 365
Leu Gly Leu Thr Asp Glu Glu Lys Glu Ala Ala Glu His Phe Leu Asn
    370                 375                 380
Val Ser Asp Asp Ser Gln Asn Asp Tyr Glu
385                 390


<210> 368
<211> 394
<212> PRT
<213> human metapneumo virus

<400> 368
Met Ser Leu Gln Gly Ile His Leu Ser Asp Leu Ser Tyr Lys His Ala
 1              5                   10                  15
Ile Leu Lys Glu Ser Gln Tyr Thr Ile Lys Arg Asp Val Gly Thr Thr
            20                  25                  30
Thr Ala Val Thr Pro Ser Ser Leu Gln Gln Glu Ile Thr Leu Leu Cys
        35                  40                  45
```

Gly Glu Ile Leu Tyr Thr Lys His Thr Asp Tyr Lys Tyr Ala Ala Glu
50 55 60
Ile Gly Ile Gln Tyr Ile Cys Thr Ala Leu Gly Ser Glu Arg Val Gln
65 70 75 80
Gln Ile Leu Arg Asn Ser Gly Ser Glu Val Gln Val Val Leu Thr Lys
85 90 95
Thr Tyr Ser Leu Gly Lys Gly Lys Asn Ser Lys Gly Glu Glu Leu Gln
100 105 110
Met Leu Asp Ile His Gly Val Glu Lys Ser Trp Ile Glu Glu Ile Asp
115 120 125
Lys Glu Ala Arg Lys Thr Met Val Thr Leu Leu Lys Glu Ser Ser Gly
130 135 140
Asn Ile Pro Gln Asn Gln Arg Pro Ser Ala Pro Asp Thr Pro Ile Ile
145 150 155 160
Leu Leu Cys Val Gly Ala Leu Ile Phe Thr Lys Leu Ala Ser Thr Ile
165 170 175
Glu Val Gly Leu Glu Thr Thr Val Arg Arg Ala Asn Arg Val Leu Ser
180 185 190
Asp Ala Leu Lys Arg Tyr Pro Arg Ile Asp Ile Pro Lys Ile Ala Arg
195 200 205
Ser Phe Tyr Glu Leu Phe Glu Gln Lys Val Tyr Tyr Arg Ser Leu Phe
210 215 220
Ile Glu Tyr Gly Lys Ala Leu Gly Ser Ser Ser Thr Gly Ser Lys Ala
225 230 235 240
Glu Ser Leu Phe Val Asn Ile Phe Met Gln Ala Tyr Gly Ala Gly Gln
245 250 255
Thr Leu Leu Arg Trp Gly Val Ile Ala Arg Ser Ser Asn Asn Ile Met
260 265 270
Leu Gly His Val Ser Val Gln Ser Glu Leu Lys Gln Val Thr Glu Val
275 280 285
Tyr Asp Leu Val Arg Glu Met Gly Pro Glu Ser Gly Leu Leu His Leu
290 295 300
Arg Gln Ser Pro Lys Ala Gly Leu Leu Ser Leu Ala Asn Cys Pro Asn
305 310 315 320
Phe Ala Ser Val Val Leu Gly Asn Ala Ser Gly Leu Gly Ile Ile Gly
325 330 335
Met Tyr Arg Gly Arg Val Pro Asn Thr Glu Leu Phe Ser Ala Ala Glu
340 345 350
Ser Tyr Ala Arg Ser Leu Lys Glu Ser Asn Lys Ile Asn Phe Ser Ser
355 360 365
Leu Gly Leu Thr Asp Glu Glu Lys Glu Ala Ala Glu His Phe Leu Asn
370 375 380
Met Ser Gly Asp Asn Gln Asn Asp Tyr Glu
385 390

<210> 369
<211> 394
<212> PRT
<213> human metapneumo virus

<400> 369
Met Ser Leu Gln Gly Ile His Leu Ser Asp Leu Ser Tyr Lys His Ala
1 5 10 15
Ile Leu Lys Glu Ser Gln Tyr Thr Ile Lys Arg Asp Val Gly Thr Thr
20 25 30
Thr Ala Val Thr Pro Ser Ser Leu Gln Gln Glu Ile Thr Leu Leu Cys
35 40 45
Gly Glu Ile Leu Tyr Thr Lys His Thr Asp Tyr Lys Tyr Ala Ala Glu
50 55 60
Ile Gly Ile Gln Tyr Ile Cys Thr Ala Leu Gly Ser Glu Arg Val Gln

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65                  70                  75                  80
Gln Ile Leu Arg Asn Ser Gly Ser Glu Val Gln Val Val Leu Thr Lys
                85                  90                  95
Thr Tyr Ser Leu Gly Lys Gly Lys Asn Ser Lys Gly Glu Glu Leu Gln
            100                 105                 110
Met Leu Asp Ile His Gly Val Glu Lys Ser Trp Val Glu Glu Ile Asp
        115                 120                 125
Lys Glu Ala Arg Lys Thr Met Val Thr Leu Leu Lys Glu Ser Ser Gly
    130                 135                 140
Asn Ile Pro Gln Asn Gln Arg Pro Ser Ala Pro Asp Thr Pro Ile Ile
145                 150                 155                 160
Leu Leu Cys Val Gly Ala Leu Ile Phe Thr Lys Leu Ala Ser Thr Ile
                165                 170                 175
Glu Val Gly Leu Glu Thr Thr Val Arg Arg Ala Asn Arg Val Leu Ser
            180                 185                 190
Asp Ala Leu Lys Arg Tyr Pro Arg Val Asp Ile Pro Lys Ile Ala Arg
        195                 200                 205
Ser Phe Tyr Glu Leu Phe Glu Gln Lys Val Tyr Tyr Arg Ser Leu Phe
    210                 215                 220
Ile Glu Tyr Gly Lys Ala Leu Gly Ser Ser Ser Thr Gly Ser Lys Ala
225                 230                 235                 240
Glu Ser Leu Phe Val Asn Ile Phe Met Gln Ala Tyr Gly Ala Gly Gln
                245                 250                 255
Thr Met Leu Arg Trp Gly Val Ile Ala Arg Ser Ser Asn Asn Ile Met
            260                 265                 270
Leu Gly His Val Ser Val Gln Ala Glu Leu Lys Gln Val Thr Glu Val
        275                 280                 285
Tyr Asp Leu Val Arg Glu Met Gly Pro Glu Ser Gly Leu Leu His Leu
    290                 295                 300
Arg Gln Ser Pro Lys Ala Gly Leu Leu Ser Leu Ala Asn Cys Pro Asn
305                 310                 315                 320
Phe Ala Ser Val Val Leu Gly Asn Ala Ser Gly Leu Gly Ile Ile Gly
                325                 330                 335
Met Tyr Arg Gly Arg Val Pro Asn Thr Glu Leu Phe Ser Ala Ala Glu
            340                 345                 350
Ser Tyr Ala Arg Ser Leu Lys Glu Ser Asn Lys Ile Asn Phe Ser Ser
        355                 360                 365
Leu Gly Leu Thr Asp Glu Glu Lys Glu Ala Ala Glu His Phe Leu Asn
    370                 375                 380
Met Ser Asp Asp Asn Gln Asp Asp Tyr Glu
385                 390
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<210> 370
<211> 1185
<212> DNA
<213> human metapneumo virus

<400> 370

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atgtctcttc aagggattca cctgagtgat ttatcataca agcatgctat attaaaagag 60
tctcagtaca caataaaaag agatgtgggt acaacaactg cagtgacacc ctcatcattg 120
caacaagaaa taacactgtt gtgtggagaa attctgtatg ctaaacatgc tgactacaaa 180
tatgctgcag aaataggaat acaatatatt agcacagctt taggatcaga gagagtgcag 240
cagattctga ggaactcagg cagtgaagtc caagtggtct taaccagaac gtactctctg 300
gggaaaatta aaaacaataa aggagaagat ttacagatgt tagacataca cggggtagag 360
aagagctggg tagaagagat agacaaagaa gcaaggaaaa caatggcaac cttgcttaag 420
gaatcatcag gtaatatccc acaaaatcag aggccctcag caccagacac acccataatc 480
ttattatgtg taggtgcctt aatattcact aaactagcat caaccataga agtgggacta 540
gagaccacag tcagaagggc taaccgtgta ctaagtgatg cactcaagag ataccctaga 600
atggacatac caaagattgc cagatccttc tatgacttat ttgaacaaaa agtgtatcac 660
agaagtttgt tcattgagta tggcaaagca ttaggctcat catctacagg cagcaaagca 720
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gaaagtctat ttgttaatat attcatgcaa gcttatgggg ccggtcaaac aatgctaagg 780
tgggggtca ttgccaggtc atccaacaat ataatgttag gacatgtatc cgtccaagct 840
gagttaaaac aggtcacaga agtctatgac ttggtgcgag aaatgggccc tgaatctgga 900
cttctacatt taaggcaaag cccaaaagct ggactgttat cactagccaa ctgtcccaac 960
tttgcaagtg ttgttctcgg aaatgcctca ggcttaggca taatcggtat gtatcgaggg 1020
agagtaccaa acacagaatt attttcagca gctgaaagtt atgccaaaag tttgaaagaa 1080
agcaataaaa taaatttctc ttcattagga cttacagatg aagagaaaga ggctgcagaa 1140
catttcttaa atgtgagtga cgacagtcaa aatgattatg agtaa 1185

<210> 371
<211> 1185
<212> DNA
<213> human metapneumo virus

<400> 371
atgtctcttc aagggattca cctgagtgat ctatcataca agcatgctat attaaaagag 60
tctcagtata caataaagag agatgtaggc acaacaaccg cagtgacacc ctcatcattg 120
caacaagaaa taacactatt gtgtggagaa attctatatg ctaagcatgc tgattacaaa 180
tatgctgcag aaataggaat acaatatatt agcacagctc taggatcaga gagagtacag 240
cagattctaa gaaactcagg tagtgaagtc caagtggttt taaccagaac gtactccttg 300
gggaaagtta aaaacaacaa aggagaagat ttacagatgt tagacataca cggagtagag 360
aaaagctggg tggaagagat agacaaagaa gcaagaaaaa caatggcaac tttgcttaaa 420
gaatcatcag gcaatattcc acaaaatcag aggccttcag caccagacac acccataatc 480
ttattatgtg taggtgcctt aatatttacc aaactagcat caactataga agtgggatta 540
gagaccacag tcagaagagc taaccgtgta ctaagtgatg cactcaaaag ataccctagg 600
atggacatac caaaaatcgc tagatctttc tatgacttat ttgaacaaaa agtgtattac 660
agaagtttgt tcattgagta tggcaaagca ttaggctcat cctctacagg cagcaaagca 720
gaaagtttat tcgttaatat attcatgcaa gcttacggtg ctggtcaaac aatgctgagg 780
tggggagtca ttgccaggtc atctaacaat ataatgttag gacatgtatc tgttcaagct 840
gagttaaaac aagtcacaga agtctatgac ctggtgcgag aaatgggccc tgaatctggg 900
ctcctacatt taaggcaaag cccaaaagct ggactgttat cactagccaa ttgtcccaac 960
tttgctagtg ttgttctcgg caatgcctca ggcttaggca taataggtat gtatcgcggg 1020
agagtgccaa acacagaact attttcagca gcagaaagct atgccaagag tttgaaagaa 1080
agcaataaaa ttaacttttc ttcattagga ctcacagatg aagaaaaaga ggctgcagaa 1140
cacttcctaa atgtgagtga cgacagtcaa aatgattatg agtaa 1185

<210> 372
<211> 1185
<212> DNA
<213> human metapneumo virus

<400> 372
atgtctcttc aagggattca cctaagtgat ctatcatata aacatgctat attaaaagag 60
tctcaataca caataaaaag agatgtaggc accacaactg cagtgacacc ttcatcatta 120
caacaagaaa taacactttt gtgtggggaa atactttaca ctaaacacac tgattacaaa 180
tatgctgctg agataggaat acaatatatt tgcacagctc taggatcaga aagagtacaa 240
cagattttga gaaactcagg tagtgaagtt caggtggttc taaccaaaac atactcctta 300
gggaaaggca aaaacagtaa aggggaagag ctgcagatgt tagatataca tggagtggaa 360
aagagttgga tagaagaaat agacaaagag gcaagaaaga caatggtaac tttgcttaag 420
gaatcatcag gtaacatccc acaaaaccag agaccttcag caccagacac accaataatt 480
ttattatgtg taggtgccct aatattcact aaactagcat caacaataga agttggatta 540
gagactacag ttagaagagc taatagagtg ctaagtgatg cactcaaaag atacccaagg 600
atagatatac caaagattgc tagatctttt tatgaactat ttgaacaaaa agtgtactac 660
agaagtttat tcattgagta cggaaaagct ttaggctcat cttcaacagg aagcaaagca 720
gaaagtttgt ttgtaaatat atttatgcaa gcttatggag ctggccaaac actgctaagg 780
tggggtgtca ttgccagatc atccaacaac ataatgctag ggcatgtatc tgtgcaatct 840
gaattgaagc aagttacaga ggtttatgac ttggtgagag aaatgggtcc tgaatctggg 900
cttttacatc taagacaaag tccaaaggca gggctgttat cattggccaa ttgccccaat 960
tttgctagtg ttgttcttgg caatgcttca ggtctaggca taatcggaat gtacagaggg 1020
agagtaccaa acacagagct attttctgca gcagaaagtt atgccagaag cttaaaagaa 1080
agcaataaaa tcaacttctc ttcgttaggg cttacagatg aagaaaaaga agctgcagaa 1140

cacttcttaa acatgagtgg tgacaatcaa aatgattatg agtaa 1185

<210> 373
<211> 1185
<212> DNA
<213> human metapneumo virus

<400> 373
atgtctcttc aagggattca cctaagtgat ctgtcatata aacatgctat attaaaagag 60
tctcaataca caataaaaag agatgtaggc accacaactg cagtgacacc ttcatcattg 120
cagcaagaga taacactttt gtgtggagag attctttaca ctaaacatac tgattacaaa 180
tatgctgcag agatagggat acaatatatt tgcacagctc taggatcaga aagagtacaa 240
cagattttaa gaaattcagg tagtgaggtt caggtggttc taaccaagac atactcttta 300
gggaaaggta aaaatagtaa aggggaagag ttgcaaatgt tagatataca tggagtggaa 360
aagagttggg tagaagaaat agacaaagag gcaagaaaaa caatggtgac tttgctaaag 420
gaatcatcag gcaacatccc acaaaaccag aggccttcag caccagacac accaataatt 480
ttattgtgtg taggtgcttt aatattcact aaactagcat caacaataga agttggacta 540
gagactacag ttagaagggc taacagagtg ttaagtgatg cgctcaaaag ataccctagg 600
gtagatatac caaagattgc tagatctttt tatgaactat ttgagcagaa agtgtattac 660
aggagtctat tcattgagta tgggaaagct ttaggctcat cttcaacagg aagcaaagca 720
gaaagtttgt ttgtaaatat atttatgcaa gcttatggag ccggtcagac aatgctaagg 780
tggggtgtca ttgccagatc atctaacaac ataatgctag ggcatgtatc tgtgcaagct 840
gaattgaaac aagttacaga ggtttatgat ttggtaagag aaatgggtcc tgaatctggg 900
cttttacatc taagacaaag tccaaaggca ggactgttat cgttggctaa ttgccccaat 960
tttgctagtg ttgttcttgg taatgcttca ggtctaggta taatcggaat gtacagggga 1020
agagtgccaa acacagagct attttctgca gcagaaagtt atgccagaag cttaaaagaa 1080
agcaacaaaa tcaacttctc ctcattaggg ctcacagacg aagaaaaaga agctgcagaa 1140
cacttcttaa acatgagtga tgacaatcaa gatgattatg agtaa 1185

<210> 374
<211> 294
<212> PRT
<213> human metapneumo virus

<400> 374
Met Ser Phe Pro Glu Gly Lys Asp Ile Leu Phe Met Gly Asn Glu Ala
1   5   10   15
Ala Lys Leu Ala Glu Ala Phe Gln Lys Ser Leu Arg Lys Pro Gly His
            20   25   30
Lys Arg Ser Gln Ser Ile Ile Gly Glu Lys Val Asn Thr Val Ser Glu
        35   40   45
Thr Leu Glu Leu Pro Thr Ile Ser Arg Pro Ala Lys Pro Thr Ile Pro
    50   55   60
Ser Glu Pro Lys Leu Ala Trp Thr Asp Lys Gly Gly Ala Thr Lys Thr
65   70   75   80
Glu Ile Lys Gln Ala Ile Lys Val Met Asp Pro Ile Glu Glu Glu Glu
                85   90   95
Ser Thr Glu Lys Lys Val Leu Pro Ser Ser Asp Gly Lys Thr Pro Ala
            100   105   110
Glu Lys Lys Leu Lys Pro Ser Thr Asn Thr Lys Lys Lys Val Ser Phe
        115   120   125
Thr Pro Asn Glu Pro Gly Lys Tyr Thr Lys Leu Glu Lys Asp Ala Leu
    130   135   140
Asp Leu Leu Ser Asp Asn Glu Glu Glu Asp Ala Glu Ser Ser Ile Leu
145   150   155   160
Thr Phe Glu Glu Arg Asp Thr Ser Ser Leu Ser Ile Glu Ala Arg Leu
                165   170   175
Glu Ser Ile Glu Glu Lys Leu Ser Met Ile Leu Gly Leu Leu Arg Thr
            180   185   190
Leu Asn Ile Ala Thr Ala Gly Pro Thr Ala Ala Arg Asp Gly Ile Arg
        195   200   205

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Asp Ala Met Ile Gly Val Arg Glu Glu Leu Ile Ala Asp Ile Ile Lys
    210                 215                 220
Glu Ala Lys Gly Lys Ala Ala Glu Met Met Glu Glu Glu Met Ser Gln
225                 230                 235                 240
Arg Ser Lys Ile Gly Asn Gly Ser Val Lys Leu Thr Glu Lys Ala Lys
                245                 250                 255
Glu Leu Asn Lys Ile Val Glu Asp Glu Ser Thr Ser Gly Glu Ser Glu
            260                 265                 270
Glu Glu Glu Glu Pro Lys Asp Thr Gln Asp Asn Ser Gln Glu Asp Asp
        275                 280                 285
Ile Tyr Gln Leu Ile Met
    290
```

<210> 375
<211> 294
<212> PRT
<213> human metapneumo virus

<400> 375

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Met Ser Phe Pro Glu Gly Lys Asp Ile Leu Phe Met Gly Asn Glu Ala
1               5                   10                  15
Ala Lys Leu Ala Glu Ala Phe Gln Lys Ser Leu Arg Lys Pro Asn His
            20                  25                  30
Lys Arg Ser Gln Ser Ile Ile Gly Glu Lys Val Asn Thr Val Ser Glu
        35                  40                  45
Thr Leu Glu Leu Pro Thr Ile Ser Arg Pro Thr Lys Pro Thr Ile Leu
    50                  55                  60
Ser Glu Pro Lys Leu Ala Trp Thr Asp Lys Gly Gly Ala Ile Lys Thr
65                  70                  75                  80
Glu Ala Lys Gln Thr Ile Lys Val Met Asp Pro Ile Glu Glu Glu Glu
                85                  90                  95
Phe Thr Glu Lys Arg Val Leu Pro Ser Ser Asp Gly Lys Thr Pro Ala
            100                 105                 110
Glu Lys Lys Leu Lys Pro Ser Thr Asn Thr Lys Lys Lys Val Ser Phe
        115                 120                 125
Thr Pro Asn Glu Pro Gly Lys Tyr Thr Lys Leu Glu Lys Asp Ala Leu
    130                 135                 140
Asp Leu Leu Ser Asp Asn Glu Glu Glu Asp Ala Glu Ser Ser Ile Leu
145                 150                 155                 160
Thr Phe Glu Glu Arg Asp Thr Ser Ser Leu Ser Ile Glu Ala Arg Leu
                165                 170                 175
Glu Ser Ile Glu Glu Lys Leu Ser Met Ile Leu Gly Leu Leu Arg Thr
            180                 185                 190
Leu Asn Ile Ala Thr Ala Gly Pro Thr Ala Ala Arg Asp Gly Ile Arg
        195                 200                 205
Asp Ala Met Ile Gly Ile Arg Glu Glu Leu Ile Ala Asp Ile Ile Lys
    210                 215                 220
Glu Ala Lys Gly Lys Ala Ala Glu Met Met Glu Glu Glu Met Asn Gln
225                 230                 235                 240
Arg Thr Lys Ile Gly Asn Gly Ser Val Lys Leu Thr Glu Lys Ala Lys
                245                 250                 255
Glu Leu Asn Lys Ile Val Glu Asp Glu Ser Thr Ser Gly Glu Ser Glu
            260                 265                 270
Glu Glu Glu Glu Pro Lys Asp Thr Gln Glu Asn Asn Gln Glu Asp Asp
        275                 280                 285
Ile Tyr Gln Leu Ile Met
    290
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<210> 376

<211> 294
<212> PRT
<213> human metapneumo virus

<400> 376
Met Ser Phe Pro Glu Gly Lys Asp Ile Leu Phe Met Gly Asn Glu Ala
1 5 10 15
Ala Lys Ile Ala Glu Ala Phe Gln Lys Ser Leu Lys Lys Ser Gly His
20 25 30
Lys Arg Thr Gln Ser Ile Val Gly Glu Lys Val Asn Thr Ile Ser Glu
35 40 45
Thr Leu Glu Leu Pro Thr Ile Ser Lys Pro Ala Arg Ser Ser Thr Leu
50 55 60
Leu Glu Pro Lys Leu Ala Trp Ala Asp Asn Ser Gly Ile Thr Lys Ile
65 70 75 80
Thr Glu Lys Pro Ala Thr Lys Thr Thr Asp Pro Val Glu Glu Glu Glu
85 90 95
Phe Asn Glu Lys Lys Val Leu Pro Ser Ser Asp Gly Lys Thr Pro Ala
100 105 110
Glu Lys Lys Ser Lys Phe Ser Thr Ser Val Lys Lys Lys Val Ser Phe
115 120 125
Thr Ser Asn Glu Pro Gly Lys Tyr Thr Lys Leu Glu Lys Asp Ala Leu
130 135 140
Asp Leu Leu Ser Asp Asn Glu Glu Glu Asp Ala Glu Ser Ser Ile Leu
145 150 155 160
Thr Phe Glu Glu Lys Asp Thr Ser Ser Leu Ser Ile Glu Ala Arg Leu
165 170 175
Glu Ser Ile Glu Glu Lys Leu Ser Met Ile Leu Gly Leu Leu Arg Thr
180 185 190
Leu Asn Ile Ala Thr Ala Gly Pro Thr Ala Ala Arg Asp Gly Ile Arg
195 200 205
Asp Ala Met Ile Gly Ile Arg Glu Glu Leu Ile Ala Glu Ile Ile Lys
210 215 220
Glu Ala Lys Gly Lys Ala Ala Glu Met Met Glu Glu Glu Met Asn Gln
225 230 235 240
Arg Ser Lys Ile Gly Asn Gly Ser Val Lys Leu Thr Glu Lys Ala Lys
245 250 255
Glu Leu Asn Lys Ile Val Glu Asp Glu Ser Thr Ser Gly Glu Ser Glu
260 265 270
Glu Glu Glu Glu Pro Lys Glu Thr Gln Asp Asn Asn Gln Gly Glu Asp
275 280 285
Ile Tyr Gln Leu Ile Met
290

<210> 377
<211> 294
<212> PRT
<213> human metapneumo virus

<400> 377
Met Ser Phe Pro Glu Gly Lys Asp Ile Leu Phe Met Gly Asn Glu Ala
1 5 10 15
Ala Lys Ile Ala Glu Ala Phe Gln Lys Ser Leu Lys Arg Ser Gly His
20 25 30
Lys Arg Thr Gln Ser Ile Val Gly Glu Lys Val Asn Thr Ile Ser Glu
35 40 45
Thr Leu Glu Leu Pro Thr Ile Ser Lys Pro Ala Arg Ser Ser Thr Leu
50 55 60
Leu Glu Pro Lys Leu Ala Trp Ala Asp Ser Ser Gly Ala Thr Lys Thr
65 70 75 80

```
Thr Glu Lys Gln Thr Thr Lys Thr Thr Asp Pro Val Glu Glu Glu Glu
                85                  90                  95
Leu Asn Glu Lys Lys Val Ser Pro Ser Ser Asp Gly Lys Thr Pro Ala
            100                 105                 110
Glu Lys Lys Ser Lys Ser Pro Thr Asn Val Lys Lys Lys Val Ser Phe
        115                 120                 125
Thr Ser Asn Glu Pro Gly Lys Tyr Thr Lys Leu Glu Lys Asp Ala Leu
    130                 135                 140
Asp Leu Leu Ser Asp Asn Glu Glu Glu Asp Ala Glu Ser Ser Ile Leu
145                 150                 155                 160
Thr Phe Glu Glu Arg Asp Thr Ser Ser Leu Ser Ile Glu Ala Arg Leu
                165                 170                 175
Glu Ser Ile Glu Glu Lys Leu Ser Met Ile Leu Gly Leu Leu Arg Thr
            180                 185                 190
Leu Asn Ile Ala Thr Ala Gly Pro Thr Ala Ala Arg Asp Gly Ile Arg
        195                 200                 205
Asp Ala Met Ile Gly Ile Arg Glu Glu Leu Ile Ala Glu Ile Ile Lys
    210                 215                 220
Glu Ala Lys Gly Lys Ala Ala Glu Met Met Glu Glu Glu Met Asn Gln
225                 230                 235                 240
Arg Ser Lys Ile Gly Asn Gly Ser Val Lys Leu Thr Glu Lys Ala Lys
                245                 250                 255
Glu Leu Asn Lys Ile Val Glu Asp Glu Ser Thr Ser Gly Glu Ser Glu
            260                 265                 270
Glu Glu Glu Glu Pro Lys Glu Thr Gln Asp Asn Asn Gln Gly Glu Asp
        275                 280                 285
Ile Tyr Gln Leu Ile Met
    290
```

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<210> 378
<211> 885
<212> DNA
<213> human metapneumo virus

<400> 378
atgtcattcc ctgaaggaaa agatattctt ttcatgggta atgaagcagc aaaattagca 60
gaagctttcc agaaatcatt aagaaaacca ggtcataaaa gatctcaatc tattatagga 120
gaaaaagtga atactgtatc agaaacattg gaattaccta ctatcagtag acctgcaaaa 180
ccaaccatac cgtcagaacc aaagttagca tggacagata aaggtggggc aaccaaaact 240
gaaataaagc aagcaatcaa agtcatggat cccattgaag aagaagagtc taccgagaag 300
aaggtgctac cctccagtga tgggaaaacc cctgcagaaa agaaactgaa accatcaact 360
aacaccaaaa agaaggtttc atttacacca aatgaaccag ggaaatatac aaagttggaa 420
aaagatgctc tagatttgct ctcagataat gaagaagaag atgcagaatc ttcaatctta 480
acctttgaag aaagagatac ttcatcatta agcattgagg ccagattgga atcaatagag 540
gagaaattaa gcatgatatt agggctatta agaacactca acattgctac agcaggaccc 600
acagcagcaa gagatgggat cagagatgca atgattggcg taagagagga attaatagca 660
gacataataa aggaagctaa agggaaagca gcagaaatga tggaagagga aatgagtcaa 720
cgatcaaaaa taggaaatgg tagtgtaaaa ttaacagaaa aagcaaaaga gctcaacaaa 780
attgttgaag atgaaagcac aagtggagaa tccgaagaag aagaagaacc aaaagacaca 840
caagacaata gtcaagaaga tgacatttac cagttaatta tgtag                885

<210> 379
<211> 885
<212> DNA
<213> human metapneumo virus

<400> 379
atgtcattcc ctgaaggaaa agatattctt ttcatgggta atgaagcagc aaaattggca 60
gaagcttttc aaaaatcatt aagaaaacct aatcataaaa gatctcaatc tattatagga 120
gaaaaagtga acactgtatc tgaaacattg gaattaccta ctatcagtag acctaccaaa 180
```

ccgaccatat tgtcagagcc gaagttagca tggacagaca aaggtggggc aatcaaaact 240
gaagcaaagc aaacaatcaa agttatggat cctattgaag aagaagagtt tactgagaaa 300
agggtgctgc cctccagtga tgggaaaact cctgcagaaa agaagttgaa accatcaacc 360
aacactaaaa agaaggtctc atttacacca aatgaaccag gaaaatacac aaagttggag 420
aaagatgctc tagacttgct ttcagacaat gaagaagaag atgcagaatc ctcaatctta 480
accttcgaag aaagagatac ttcatcatta agcattgaag ccagactaga atcgattgag 540
gagaaattaa gcatgatatt agggctatta agaacactca acattgctac agcaggaccc 600
acagcagcaa gagatgggat cagagatgca atgattggca taagggagga actaatagca 660
gacataataa aagaagccaa gggaaaagca gcagaaatga tggaagaaga aatgaaccag 720
cggacaaaaa taggaaacgg tagtgtaaaa ttaactgaaa aggcaaagga gctcaacaaa 780
attgttgaag acgaaagcac aagtggtgaa tccgaagaag aagaagaacc aaaagacaca 840
caggaaaata atcaagaaga tgacatttac cagttaatta tgtag 885

<210> 380
<211> 885
<212> DNA
<213> human metapneumo virus

<400> 380
atgtcattcc ctgaaggaaa ggatattctg ttcatgggta atgaagcagc aaaaatagcc 60
gaagctttcc agaaatcact gaaaaaatca ggtcacaaga gaactcaatc tattgtaggg 120
gaaaaagtta acactatatc agaaactcta gaactaccta ccatcagcaa acctgcacga 180
tcatctacac tgctggaacc aaaattggca tgggcagaca acagcggaat caccaaaatc 240
acagaaaaac cagcaaccaa aacaacagat cctgttgaag aagaggaatt caatgaaaag 300
aaagtgttac cttccagtga tgggaagact cctgcagaga aaaaatcaaa gttttcaacc 360
agtgtaaaaa agaaagtttc ctttacatca aatgaaccag ggaaatacac caaactagag 420
aaagatgccc tagatttgct ctcagacaat gaggaagaag acgcagaatc ctcaatccta 480
acttttgagg agaaagatac atcatcacta agcattgaag ctagactaga atctatagaa 540
gagaagttga gcatgatatt aggactgctt cgtacactta acattgcaac agcaggacca 600
acagctgcac gagatggaat tagggatgca atgattggta taagagaaga gctaatagca 660
gagataatta aggaagccaa gggaaaagca gctgaaatga tggaagaaga gatgaatcaa 720
agatcaaaaa taggaaatgg cagtgtaaaa ctaaccgaga aggcaaaaga gctcaacaaa 780
attgttgaag acgagagcac aagcggtgaa tcagaagaag aagaagaacc aaaagaaact 840
caggataaca atcaaggaga agatatttat cagttaatca tgtag 885

<210> 381
<211> 885
<212> DNA
<213> human metapneumo virus

<400> 381
atgtcattcc ctgaaggaaa agatatcctg ttcatgggta atgaagcagc aaaaatagca 60
gaagctttcc agaaatcact aaaaagatca ggtcacaaaa gaacccagtc tattgtaggg 120
gaaaaagtaa acactatatc agaaactcta gagctaccta ccatcagcaa acctgcacga 180
tcatctacac tgctagagcc aaaattggca tgggcagaca gcagcggagc caccaaaacc 240
acagaaaaac aaacaaccaa aacaacagat cctgttgaag aagaggaact caatgaaaag 300
aaggtatcac cttccagtga tgggaagact cctgcagaga aaaaatcaaa atctccaacc 360
aatgtaaaaa agaaagtttc cttcacatca aatgaaccag ggaaatatac taaactagaa 420
aaagatgccc tagatttgct ctcagacaat gaggaagaag acgcagagtc ctcaatccta 480
acctttgaag agagagacac atcatcacta agcattgagg ctagactaga atcaatagaa 540
gagaagctaa gcatgatatt aggactgctt cgtacactta acattgcaac agcaggacca 600
acggctgcaa gggatggaat cagagatgca atgattggta taagagaaga actaatagca 660
gaaataataa aagaagcaaa gggaaaagca gccgaaatga tggaagagga aatgaatcaa 720
aggtcaaaaa taggtaatgg cagtgtaaaa ctaaccgaga aggcaaaaga acttaataaa 780
attgttgaag acgagagcac aagtggtgaa tcagaagaag aagaagaacc aaaagaaact 840
caggataaca atcaaggaga agatatctac cagttaatca tgtag 885

<210> 382
<211> 183
<212> PRT
<213> human metapneumo virus

<400> 382
Met Ile Thr Leu Asp Val Ile Lys Ser Asp Gly Ser Ser Lys Thr Cys
1 5 10 15
Thr His Leu Lys Lys Ile Ile Lys Asp His Ser Gly Lys Val Leu Ile
20 25 30
Val Leu Lys Leu Ile Leu Ala Leu Leu Thr Phe Leu Thr Val Thr Ile
35 40 45
Thr Ile Asn Tyr Ile Lys Val Glu Asn Asn Leu Gln Ile Cys Gln Ser
50 55 60
Lys Thr Glu Ser Asp Lys Lys Asp Ser Ser Ser Asn Thr Thr Ser Val
65 70 75 80
Thr Thr Lys Thr Thr Leu Asn His Asp Ile Thr Gln Tyr Phe Lys Ser
85 90 95
Leu Ile Gln Arg Tyr Thr Asn Ser Ala Ile Asn Ser Asp Thr Cys Trp
100 105 110
Lys Ile Asn Arg Asn Gln Cys Thr Asn Ile Thr Thr Tyr Lys Phe Leu
115 120 125
Cys Phe Lys Ser Glu Asp Thr Lys Thr Asn Asn Cys Asp Lys Leu Thr
130 135 140
Asp Leu Cys Arg Asn Lys Pro Lys Pro Ala Val Gly Val Tyr His Ile
145 150 155 160
Val Glu Cys His Cys Ile Tyr Thr Val Lys Trp Lys Cys Tyr His Tyr
165 170 175
Pro Thr Asp Glu Thr Gln Ser
180

<210> 383
<211> 179
<212> PRT
<213> human metapneumo virus

<400> 383
Met Ile Thr Leu Asp Val Ile Lys Ser Asp Gly Ser Ser Lys Thr Cys
1 5 10 15
Thr His Leu Lys Lys Ile Ile Lys Asp His Ser Gly Lys Val Leu Ile
20 25 30
Ala Leu Lys Leu Ile Leu Ala Leu Leu Thr Phe Phe Thr Ile Thr Ile
35 40 45
Thr Ile Asn Tyr Ile Lys Val Glu Asn Asn Leu Gln Ile Cys Gln Ser
50 55 60
Lys Thr Glu Ser Asp Lys Glu Asp Ser Pro Ser Asn Thr Thr Ser Val
65 70 75 80
Thr Thr Lys Thr Thr Leu Asp His Asp Ile Thr Gln Tyr Phe Lys Arg
85 90 95
Leu Ile Gln Arg Tyr Thr Asp Ser Val Ile Asn Lys Asp Thr Cys Trp
100 105 110
Lys Ile Ser Arg Asn Gln Cys Thr Asn Ile Thr Thr Tyr Lys Phe Leu
115 120 125
Cys Phe Lys Pro Glu Asp Ser Lys Ile Asn Ser Cys Asp Arg Leu Thr
130 135 140
Asp Leu Cys Arg Asn Lys Ser Lys Ser Ala Ala Glu Ala Tyr His Thr
145 150 155 160
Val Glu Cys His Cys Ile Tyr Thr Ile Glu Trp Lys Cys Tyr His His
165 170 175
Pro Ile Asp

<210> 384

<211> 177
<212> PRT
<213> human metapneumo virus

<400> 384
Met Lys Thr Leu Asp Val Ile Lys Ser Asp Gly Ser Ser Glu Thr Cys
1 5 10 15
Asn Gln Leu Lys Lys Ile Ile Lys Lys His Ser Gly Lys Val Leu Ile
20 25 30
Ala Leu Lys Leu Ile Leu Ala Leu Leu Thr Phe Phe Thr Ala Thr Ile
35 40 45
Thr Val Asn Tyr Ile Lys Val Glu Asn Asn Leu Gln Ala Cys Gln Pro
50 55 60
Lys Asn Glu Ser Asp Lys Lys Val Thr Lys Pro Asn Thr Thr Ser Thr
65 70 75 80
Thr Ile Arg Pro Thr Pro Asp Pro Thr Val Val His His Leu Lys Arg
85 90 95
Leu Ile Gln Arg His Thr Asn Ser Val Thr Lys Asp Ser Asp Thr Cys
100 105 110
Trp Arg Ile His Lys Asn Gln Arg Thr Asn Ile Lys Ile Tyr Lys Phe
115 120 125
Leu Cys Ser Gly Phe Thr Asn Ser Lys Gly Thr Asp Cys Glu Glu Pro
130 135 140
Thr Ala Leu Cys Asp Lys Lys Leu Lys Thr Ile Val Glu Lys His Arg
145 150 155 160
Lys Ala Glu Cys His Cys Leu His Thr Thr Glu Trp Gly Cys Leu His
165 170 175
Pro

<210> 385
<211> 177
<212> PRT
<213> human metapneumo virus

<400> 385
Met Lys Thr Leu Asp Val Ile Lys Ser Asp Gly Ser Ser Glu Thr Cys
1 5 10 15
Asn Gln Leu Lys Lys Ile Ile Lys Lys His Ser Gly Lys Leu Leu Ile
20 25 30
Ala Leu Lys Leu Ile Leu Ala Leu Leu Thr Phe Phe Thr Val Thr Ile
35 40 45
Thr Val Asn Tyr Ile Lys Val Glu Asn Asn Leu Gln Ala Cys Gln Leu
50 55 60
Lys Asn Glu Ser Asp Lys Lys Asp Thr Lys Leu Asn Thr Thr Ser Thr
65 70 75 80
Thr Ile Arg Pro Ile Pro Asp Leu Asn Ala Val Gln Tyr Leu Lys Arg
85 90 95
Leu Ile Gln Lys His Thr Asn Phe Val Ile Lys Asp Arg Asp Thr Cys
100 105 110
Trp Arg Ile His Thr Asn Gln Cys Thr Asn Ile Lys Ile Tyr Lys Phe
115 120 125
Leu Cys Phe Gly Phe Met Asn Ser Thr Asn Thr Asp Cys Glu Glu Leu
130 135 140
Thr Val Leu Cys Asp Lys Lys Ser Lys Thr Met Thr Glu Lys His Arg
145 150 155 160
Lys Ala Glu Cys His Cys Leu His Thr Thr Glu Trp Trp Cys Tyr Tyr
165 170 175
Leu

<210> 386
<211> 552
<212> DNA
<213> human metapneumo virus

<400> 386
atgataacat tagatgtcat taaaagtgat gggtcttcaa aaacatgtac tcacctcaaa 60
aaaataatta aagaccactc tggtaaagtg cttattgtac ttaagttaat attagcttta 120
ctaacatttc tcacagtaac aatcaccatc aattatataa aagtggaaaa caatctgcaa 180
atatgccagt caaaaactga atcagacaaa aaggactcat catcaaatac cacatcagtc 240
acaaccaaga ctactctaaa tcatgatatc acacagtatt ttaaaagttt gattcaaagg 300
tatacaaact ctgcaataaa cagtgacaca tgctggaaaa taaacagaaa tcaatgcaca 360
aatataacaa catacaaatt tttatgtttt aaatctgaag acacaaaaac caacaattgt 420
gataaactga cagatttatg cagaaacaaa ccaaaaccag cagttggagt gtatcacata 480
gtagaatgcc attgtatata cacagttaaa tggaagtgct atcattaccc aaccgatgaa 540
acccaatcct aa 552

<210> 387
<211> 540
<212> DNA
<213> human metapneumo virus

<400> 387
atgataacat tagatgtcat taaaagtgat gggtcttcaa aaacatgtac tcacctcaaa 60
aaaataatca aagaccattc tggtaaagtg cttattgcac ttaagttaat attagcttta 120
ctaacatttt tcacaataac aatcactata aattacataa aagtagaaaa caatctacaa 180
atatgccagt caaaaactga atcagacaaa gaagactcac catcaaatac cacatccgtc 240
acaaccaaga ctactctaga ccatgatata acacagtatt ttaaaagatt aattcaaagg 300
tatacagatt ctgtgataaa caaggacaca tgctggaaaa taagcagaaa tcaatgcaca 360
aatataacaa catataaatt tttatgcttt aaacctgagg actcaaaaat caacagttgt 420
gatagactga cagatctatg cagaaacaaa tcaaaatcag cagctgaagc atatcataca 480
gtagaatgcc attgcatata cacaattgag tggaagtgct atcaccaccc aatagattaa 540

<210> 388
<211> 534
<212> DNA
<213> human metapneumo virus

<400> 388
atgaaaacat tagatgtcat aaaaagtgat ggatcctcag aaacgtgtaa tcaactcaaa 60
aaaataataa aaaaacactc aggtaaagtg cttattgcac taaaactgat attggcctta 120
ctgacatttt tcacagcaac aatcactgtc aactatataa aagtagaaaa caatttgcag 180
gcatgtcaac caaaaaatga atcagacaaa aaggtcacaa agccaaatac cacatcaaca 240
acaatcagac ccacacccga tccaactgta gtacatcatt tgaaaaggct gattcagaga 300
cacaccaact ctgtcacaaa agacagcgat acttgttgga gaatacacaa gaatcaacgt 360
acaaatataa aaatatacaa gttcttatgc tctgggttca caaattcaaa aggtacagat 420
tgtgaggaac caacagccct atgcgacaaa aagttaaaaa ccatagtaga aaaacataga 480
aaagcagaat gtcactgtct acatacaacc gagtgggggt gccttcatcc ctaa 534

<210> 389
<211> 534
<212> DNA
<213> human metapneumo virus

<400> 389
atgaaaacat tagatgtcat aaaaagtgat ggatcctcag aaacatgtaa tcaactcaaa 60
aaaataataa aaaaacactc aggtaaattg cttattgcat taaaactgat attggcctta 120
ttgacgtttt tcacagtaac aattactgtt aactatataa aagtagaaaa caatttgcag 180

gcatgtcaat taaaaaatga atcagacaaa aaggacacaa agctaaatac cacatcaaca 240
acaatcagac ccattcctga tctaaatgca gtacagtact tgaaaaggct gattcagaaa 300
cacaccaact ttgtcataaa agacagagat acctgttgga gaatacacac gaatcaatgc 360
acaaatataa aaatatataa gttcttatgt ttcgggttta tgaattcaac aaatacagac 420
tgtgaagaac taacagtttt atgtgataaa aagtcaaaaa ccatgacaga aaaacatagg 480
aaagcagagt gtcactgtct acatacaacc gagtggtggt gttattatct ttaa 534

<210> 390
<211> 298
<212> PRT
<213> Human respiratory syncytial virus

<220>
<223> attachment glycoprotein of Human respiratory syncytial virus

<400> 390
Met Ser Lys Thr Lys Asp Gln Arg Thr Ala Lys Thr Leu Glu Arg Thr
1 5 10 15
Trp Asp Thr Leu Asn His Leu Leu Phe Ile Ser Ser Cys Leu Tyr Lys
20 25 30
Leu Asn Leu Lys Ser Ile Ala Gln Ile Thr Leu Ser Ile Leu Ala Met
35 40 45
Ile Ile Ser Thr Ser Leu Ile Ile Ala Ala Ile Ile Phe Ile Ala Ser
50 55 60
Ala Asn His Lys Val Thr Leu Thr Thr Ala Ile Ile Gln Asp Ala Thr
65 70 75 80
Asn Gln Ile Lys Asn Thr Thr Pro Thr Tyr Leu Thr Gln Asn Pro Gln
85 90 95
Leu Gly Ile Ser Phe Ser Asn Leu Ser Glu Thr Thr Ser Gln Pro Ile
100 105 110
Thr Ile Leu Ala Ser Thr Thr Pro Ser Ala Glu Ser Thr Pro Gln Ser
115 120 125
Thr Thr Val Lys Thr Lys Asn Thr Thr Thr Thr Gln Ile Gln Pro Ser
130 135 140
Lys Ser Thr Thr Lys Gln Arg Gln Asn Lys Pro Gln Asn Lys Pro Asn
145 150 155 160
Asn Asp Phe His Phe Glu Val Phe Asn Phe Val Pro Cys Ser Ile Cys
165 170 175
Ser Asn Asn Pro Thr Cys Trp Ala Ile Cys Lys Arg Ile Pro Asn Lys
180 185 190
Lys Pro Gly Lys Lys Thr Thr Thr Lys Pro Thr Lys Lys Pro Thr Ile
195 200 205
Lys Thr Thr Lys Lys Asp Leu Lys Pro Gln Thr Thr Lys Ser Lys Glu
210 215 220
Val Leu Thr Thr Lys Pro Thr Glu Lys Pro Thr Ile Asn Thr Thr Lys
225 230 235 240
Thr Asn Ile Arg Thr Thr Leu Leu Ile Ser Asn Thr Thr Gly Asn Pro
245 250 255
Glu His Thr Ser Gln Lys Glu Thr Leu His Ser Thr Thr Ser Glu Gly
260 265 270
Asn Pro Ser Pro Ser Gln Val Tyr Thr Thr Ser Glu Tyr Leu Ser Gln
275 280 285
Ser Leu Ser Pro Ser Asn Thr Thr Tyr Tyr
290 295

<210> 391
<211> 574
<212> PRT
<213> Human respiratory syncytial virus

<220>
<223> fusion glycoprotein of Human respiratory syncytial virus

<400> 391
Met Glu Leu Pro Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Ala
1 5 10 15
Ala Val Thr Leu Cys Phe Val Ser Ser Gln Asn Ile Thr Glu Glu Phe
20 25 30
Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45
Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60
Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80
Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95
Met Gln Ser Thr Pro Ala Ala Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110
Arg Phe Met Asn Tyr Thr Leu Asn Asn Thr Lys Asn Thr Asn Val Thr
115 120 125
Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140
Gly Ser Ala Ile Ala Ser Gly Ile Ala Val Ser Lys Val Leu His Leu
145 150 155 160
Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
165 170 175
Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190
Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
195 200 205
Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220
Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240
Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255
Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270
Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285
Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300
Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320
Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335
Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350
Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
355 360 365
Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
370 375 380
Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400
Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415
Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430
Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450   455   460
Lys Asn Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465   470   475   480
Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485   490   495
Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500   505   510
Leu His Asn Val Asn Ala Gly Lys Ser Thr Thr Asn Ile Met Ile Thr
        515   520   525
Thr Ile Ile Ile Val Ile Ile Val Ile Leu Leu Ser Leu Ile Ala Val
    530   535   540
Gly Leu Leu Leu Tyr Cys Lys Ala Arg Ser Thr Pro Val Thr Leu Ser
545   550   555   560
Lys Asp Gln Leu Ser Gly Ile Asn Asn Ile Ala Phe Ser Ser
                565   570

<210> 392
<211> 64
<212> PRT
<213> Human respiratory syncytial virus

<220>
<223> small hydrophobic protein of Human respiratory syncytial virus

<400> 392
Met Glu Asn Thr Ser Ile Thr Ile Glu Phe Ser Ser Lys Phe Trp Pro
1   5   10   15
Tyr Phe Thr Leu Ile His Met Ile Thr Thr Ile Ile Ser Leu Leu Ile
            20   25   30
Ile Ile Ser Ile Met Ile Ala Ile Leu Asn Lys Leu Cys Glu Tyr Asn
        35   40   45
Ala Phe His Asn Lys Thr Phe Glu Leu Pro Arg Ala Arg Ile Asn Thr
    50   55   60

<210> 393
<211> 2165
<212> PRT
<213> Human respiratory syncytial virus (strain A2)

<220>
<223> RNA polymerase beta subunit (Large structural protein) (L protein) of Human respiratory syncytial virus

<400> 393
Met Asp Pro Ile Ile Asn Gly Asn Ser Ala Asn Val Tyr Leu Thr Asp
1   5   10   15
Ser Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Cys Asn Ala Leu Gly
            20   25   30
Ser Tyr Ile Phe Asn Gly Pro Tyr Leu Lys Asn Asp Tyr Thr Asn Leu
        35   40   45
Ile Ser Arg Gln Asn Pro Leu Ile Glu His Met Asn Leu Lys Lys Leu
    50   55   60
Asn Ile Thr Gln Ser Leu Ile Ser Lys Tyr His Lys Gly Glu Ile Lys
65   70   75   80
Leu Glu Glu Pro Thr Tyr Phe Gln Ser Leu Leu Met Thr Tyr Lys Ser
                85   90   95
Met Thr Ser Ser Glu Gln Ile Ala Thr Thr Asn Leu Leu Lys Lys Ile
            100   105   110

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Ile Arg Arg Ala Ile Glu Ile Ser Asp Val Lys Val Tyr Ala Ile Leu
        115                 120                 125
Asn Lys Leu Gly Leu Lys Glu Lys Asp Lys Ile Lys Ser Asn Asn Gly
    130                 135                 140
Gln Asp Glu Asp Asn Ser Val Ile Thr Thr Ile Ile Lys Asp Asp Ile
145                 150                 155                 160
Leu Ser Ala Val Lys Asp Asn Gln Ser His Leu Lys Ala Asp Lys Asn
                165                 170                 175
His Ser Thr Lys Gln Lys Asp Thr Ile Lys Thr Thr Leu Leu Lys Lys
            180                 185                 190
Leu Met Cys Ser Met Gln His Pro Pro Ser Trp Leu Ile His Trp Phe
        195                 200                 205
Asn Leu Tyr Thr Lys Leu Asn Asn Ile Leu Thr Gln Tyr Arg Ser Asn
    210                 215                 220
Glu Val Lys Asn His Gly Phe Thr Leu Ile Asp Asn Gln Thr Leu Ser
225                 230                 235                 240
Gly Phe Gln Phe Ile Leu Asn Gln Tyr Gly Cys Ile Val Tyr His Lys
                245                 250                 255
Glu Leu Lys Arg Ile Thr Val Thr Thr Tyr Asn Gln Phe Leu Thr Trp
            260                 265                 270
Lys Asp Ile Ser Leu Ser Arg Leu Asn Val Cys Leu Ile Thr Trp Ile
        275                 280                 285
Ser Asn Cys Leu Asn Thr Leu Asn Lys Ser Leu Gly Leu Arg Cys Gly
    290                 295                 300
Phe Asn Asn Val Ile Leu Thr Gln Leu Phe Leu Tyr Gly Asp Cys Ile
305                 310                 315                 320
Leu Lys Leu Phe His Asn Glu Gly Phe Tyr Ile Ile Lys Glu Val Glu
                325                 330                 335
Gly Phe Ile Met Ser Leu Ile Leu Asn Ile Thr Glu Glu Asp Gln Phe
            340                 345                 350
Arg Lys Arg Phe Tyr Asn Ser Met Leu Asn Asn Ile Thr Asp Ala Ala
        355                 360                 365
Asn Lys Ala Gln Lys Asn Leu Leu Ser Arg Val Cys His Thr Leu Leu
    370                 375                 380
Asp Lys Thr Val Ser Asp Asn Ile Ile Asn Gly Arg Trp Ile Ile Leu
385                 390                 395                 400
Leu Ser Lys Phe Leu Lys Leu Ile Lys Leu Ala Gly Asp Asn Asn Leu
                405                 410                 415
Asn Asn Leu Ser Glu Leu Tyr Phe Leu Phe Arg Ile Phe Gly His Pro
            420                 425                 430
Met Val Asp Glu Arg Gln Ala Met Asp Ala Val Lys Ile Asn Cys Asn
        435                 440                 445
Glu Thr Lys Phe Tyr Leu Leu Ser Ser Leu Ser Met Leu Arg Gly Ala
    450                 455                 460
Phe Ile Tyr Arg Ile Ile Lys Gly Phe Val Asn Asn Tyr Asn Arg Trp
465                 470                 475                 480
Pro Thr Leu Arg Asn Ala Ile Val Leu Pro Leu Arg Trp Leu Thr Tyr
                485                 490                 495
Tyr Lys Leu Asn Thr Tyr Pro Ser Leu Leu Glu Leu Thr Glu Arg Asp
            500                 505                 510
Leu Ile Val Leu Ser Gly Leu Arg Phe Tyr Arg Glu Phe Arg Leu Pro
        515                 520                 525
Lys Lys Val Asp Leu Glu Met Ile Ile Asn Asp Lys Ala Ile Ser Pro
    530                 535                 540
Pro Lys Asn Leu Ile Trp Thr Ser Phe Pro Arg Asn Tyr Met Pro Ser
545                 550                 555                 560
His Ile Gln Asn Tyr Ile Glu His Glu Lys Leu Lys Phe Ser Glu Ser
                565                 570                 575
Asp Lys Ser Arg Arg Val Leu Glu Tyr Tyr Leu Arg Asp Asn Lys Phe
            580                 585                 590
Asn Glu Cys Asp Leu Tyr Asn Cys Val Val Asn Gln Ser Tyr Leu Asn
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        595                 600                 605
Asn Pro Asn His Val Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser
    610                 615                 620
Val Gly Arg Met Phe Ala Met Gln Pro Gly Met Phe Arg Gln Val Gln
625                 630                 635                 640
Ile Leu Ala Glu Lys Met Ile Ala Glu Asn Ile Leu Gln Phe Phe Pro
                645                 650                 655
Glu Ser Leu Thr Arg Tyr Gly Asp Leu Glu Leu Gln Lys Ile Leu Glu
            660                 665                 670
Leu Lys Ala Gly Ile Ser Asn Lys Ser Asn Arg Tyr Asn Asp Asn Tyr
        675                 680                 685
Asn Asn Tyr Ile Ser Lys Cys Ser Ile Ile Thr Asp Leu Ser Lys Phe
    690                 695                 700
Asn Gln Ala Phe Arg Tyr Glu Thr Ser Cys Ile Cys Ser Asp Val Leu
705                 710                 715                 720
Asp Glu Leu His Gly Val Gln Ser Leu Phe Ser Trp Leu His Leu Thr
                725                 730                 735
Ile Pro His Val Thr Ile Ile Cys Thr Tyr Arg His Ala Pro Pro Tyr
            740                 745                 750
Ile Gly Asp His Ile Val Asp Leu Asn Asn Val Asp Glu Gln Ser Gly
        755                 760                 765
Leu Tyr Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu
    770                 775                 780
Trp Thr Ile Glu Ala Ile Ser Leu Leu Asp Leu Ile Ser Leu Lys Gly
785                 790                 795                 800
Lys Phe Ser Ile Thr Ala Leu Ile Asn Gly Asp Asn Gln Ser Ile Asp
                805                 810                 815
Ile Ser Lys Pro Ile Arg Leu Met Glu Gly Gln Thr His Ala Gln Ala
            820                 825                 830
Asp Tyr Leu Leu Ala Leu Asn Ser Leu Lys Leu Leu Tyr Lys Glu Tyr
        835                 840                 845
Ala Gly Ile Gly His Lys Leu Lys Gly Thr Glu Thr Tyr Ile Ser Arg
    850                 855                 860
Asp Met Gln Phe Met Ser Lys Thr Ile Gln His Asn Gly Val Tyr Tyr
865                 870                 875                 880
Pro Ala Ser Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr
                885                 890                 895
Ile Leu Asp Asp Phe Lys Val Ser Leu Glu Ser Ile Gly Ser Leu Thr
            900                 905                 910
Gln Glu Leu Glu Tyr Arg Gly Glu Ser Leu Leu Cys Ser Leu Ile Phe
        915                 920                 925
Arg Asn Val Trp Leu Tyr Asn Gln Ile Ala Leu Gln Leu Lys Asn His
    930                 935                 940
Ala Leu Cys Asn Asn Lys Leu Tyr Leu Asp Ile Leu Lys Val Leu Lys
945                 950                 955                 960
His Leu Lys Thr Phe Phe Asn Leu Asp Asn Ile Asp Thr Ala Leu Thr
                965                 970                 975
Leu Tyr Met Asn Leu Pro Met Leu Phe Gly Gly Gly Asp Pro Asn Leu
            980                 985                 990
Leu Tyr Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala
        995                 1000                1005
Ile Val His Ser Val Phe Ile Leu Ser Tyr Tyr Thr Asn His Asp Leu
    1010                1015                1020
Lys Asp Lys Leu Gln Asp Leu Ser Asp Asp Arg Leu Asn Lys Phe Leu
1025                1030                1035                1040
Thr Cys Ile Ile Thr Phe Asp Lys Asn Pro Asn Ala Glu Phe Val Thr
                1045                1050                1055
Leu Met Arg Asp Pro Gln Ala Leu Gly Ser Glu Arg Gln Ala Lys Ile
            1060                1065                1070
Thr Ser Glu Ile Asn Arg Leu Ala Val Thr Glu Val Leu Ser Thr Ala
        1075                1080                1085
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Pro Asn Lys Ile Phe Ser Lys Ser Ala Gln His Tyr Thr Thr Thr Glu
    1090                1095                1100
Ile Asp Leu Asn Asp Ile Met Gln Asn Ile Glu Pro Thr Tyr Pro His
1105                1110                1115                1120
Gly Leu Arg Val Val Tyr Glu Ser Leu Pro Phe Tyr Lys Ala Glu Lys
                1125                1130                1135
Ile Val Asn Leu Ile Ser Gly Thr Lys Ser Ile Thr Asn Ile Leu Glu
            1140                1145                1150
Lys Thr Ser Ala Ile Asp Leu Thr Asp Ile Asp Arg Ala Thr Glu Met
        1155                1160                1165
Met Arg Lys Asn Ile Thr Leu Leu Ile Arg Ile Leu Pro Leu Asp Cys
    1170                1175                1180
Asn Arg Asp Lys Arg Glu Ile Leu Ser Met Glu Asn Leu Ser Ile Thr
1185                1190                1195                1200
Glu Leu Ser Lys Tyr Val Arg Glu Arg Ser Trp Ser Leu Ser Asn Ile
                1205                1210                1215
Val Gly Val Thr Ser Pro Ser Ile Met Tyr Thr Met Asp Ile Lys Tyr
            1220                1225                1230
Thr Thr Ser Thr Ile Ser Ser Gly Ile Ile Ile Glu Lys Tyr Asn Val
        1235                1240                1245
Asn Ser Leu Thr Arg Gly Glu Arg Gly Pro Thr Lys Pro Trp Val Gly
    1250                1255                1260
Ser Ser Thr Gln Glu Lys Lys Thr Met Pro Val Tyr Asn Arg Gln Val
1265                1270                1275                1280
Leu Thr Lys Lys Gln Arg Asp Gln Ile Asp Leu Leu Ala Lys Leu Asp
                1285                1290                1295
Trp Val Tyr Ala Ser Ile Asp Asn Lys Asp Glu Phe Met Glu Glu Leu
            1300                1305                1310
Ser Ile Gly Thr Leu Gly Leu Thr Tyr Glu Lys Ala Lys Lys Leu Phe
        1315                1320                1325
Pro Gln Tyr Leu Ser Val Asn Tyr Leu His Arg Leu Thr Val Ser Ser
    1330                1335                1340
Arg Pro Cys Glu Phe Pro Ala Ser Ile Pro Ala Tyr Arg Thr Thr Asn
1345                1350                1355                1360
Tyr His Phe Asp Thr Ser Pro Ile Asn Arg Ile Leu Thr Glu Lys Tyr
                1365                1370                1375
Gly Asp Glu Asp Ile Asp Ile Val Phe Gln Asn Cys Ile Ser Phe Gly
            1380                1385                1390
Leu Ser Leu Met Ser Val Val Glu Gln Phe Thr Asn Val Cys Pro Asn
        1395                1400                1405
Arg Ile Ile Leu Ile Pro Lys Leu Asn Glu Ile His Leu Met Lys Pro
    1410                1415                1420
Pro Ile Phe Thr Gly Asp Val Asp Ile His Lys Leu Lys Gln Val Ile
1425                1430                1435                1440
Gln Lys Gln His Met Phe Leu Pro Asp Lys Ile Ser Leu Thr Gln Tyr
                1445                1450                1455
Val Glu Leu Phe Leu Ser Asn Lys Thr Leu Lys Ser Gly Ser His Val
            1460                1465                1470
Asn Ser Asn Leu Ile Leu Ala His Lys Ile Ser Asp Tyr Phe His Asn
        1475                1480                1485
Thr Tyr Ile Leu Ser Thr Asn Leu Ala Gly His Trp Ile Leu Ile Ile
    1490                1495                1500
Gln Leu Met Lys Asp Ser Lys Gly Ile Phe Glu Lys Asp Trp Gly Glu
1505                1510                1515                1520
Gly Tyr Ile Thr Asp His Met Phe Ile Asn Leu Lys Val Phe Phe Asn
                1525                1530                1535
Ala Tyr Lys Thr Tyr Leu Leu Cys Phe His Lys Gly Tyr Gly Lys Ala
            1540                1545                1550
Lys Leu Glu Cys Asp Met Asn Thr Ser Asp Leu Leu Cys Val Leu Glu
        1555                1560                1565
Leu Ile Asp Ser Ser Tyr Trp Lys Ser Met Ser Lys Val Phe Leu Glu
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1570 1575 1580
Gln Lys Val Ile Lys Tyr Ile Leu Ser Gln Asp Ala Ser Leu His Arg
1585 1590 1595 1600
Val Lys Gly Cys His Ser Phe Lys Leu Trp Phe Leu Lys Arg Leu Asn
1605 1610 1615
Val Ala Glu Phe Thr Val Cys Pro Trp Val Val Asn Ile Asp Tyr His
1620 1625 1630
Pro Thr His Met Lys Ala Ile Leu Thr Tyr Ile Asp Leu Val Arg Met
1635 1640 1645
Gly Leu Ile Asn Ile Asp Arg Ile His Ile Lys Asn Lys His Lys Phe
1650 1655 1660
Asn Asp Glu Phe Tyr Thr Ser Asn Leu Phe Tyr Ile Asn Tyr Asn Phe
1665 1670 1675 1680
Ser Asp Asn Thr His Leu Leu Thr Lys His Ile Arg Ile Ala Asn Ser
1685 1690 1695
Glu Leu Glu Asn Asn Tyr Asn Lys Leu Tyr His Pro Thr Pro Glu Thr
1700 1705 1710
Leu Glu Asn Ile Leu Ala Asn Pro Ile Lys Ser Asn Asp Lys Lys Thr
1715 1720 1725
Leu Asn Asp Tyr Cys Ile Gly Lys Asn Val Asp Ser Ile Met Leu Pro
1730 1735 1740
Leu Leu Ser Asn Lys Lys Leu Ile Lys Ser Ser Ala Met Ile Arg Thr
1745 1750 1755 1760
Asn Tyr Ser Lys Gln Asp Leu Tyr Asn Leu Phe Pro Met Val Val Ile
1765 1770 1775
Asp Arg Ile Ile Asp His Ser Gly Asn Thr Ala Lys Ser Asn Gln Leu
1780 1785 1790
Tyr Thr Thr Thr Ser His Gln Ile Ser Leu Val His Asn Ser Thr Ser
1795 1800 1805
Leu Tyr Cys Met Leu Pro Trp His His Ile Asn Arg Phe Asn Phe Val
1810 1815 1820
Phe Ser Ser Thr Gly Cys Lys Ile Ser Ile Glu Tyr Ile Leu Lys Asp
1825 1830 1835 1840
Leu Lys Ile Lys Asp Pro Asn Cys Ile Ala Phe Ile Gly Glu Gly Ala
1845 1850 1855
Gly Asn Leu Leu Leu Arg Thr Val Val Glu Leu His Pro Asp Ile Arg
1860 1865 1870
Tyr Ile Tyr Arg Ser Leu Lys Asp Cys Asn Asp His Ser Leu Pro Ile
1875 1880 1885
Glu Phe Leu Arg Leu Tyr Asn Gly His Ile Asn Ile Asp Tyr Gly Glu
1890 1895 1900
Asn Leu Thr Ile Pro Ala Thr Asp Ala Thr Asn Asn Ile His Trp Ser
1905 1910 1915 1920
Tyr Leu His Ile Lys Phe Ala Glu Pro Ile Ser Leu Phe Val Cys Asp
1925 1930 1935
Ala Glu Leu Ser Val Thr Val Asn Trp Ser Lys Ile Ile Ile Glu Trp
1940 1945 1950
Ser Lys His Val Arg Lys Cys Lys Tyr Cys Ser Ser Val Asn Lys Cys
1955 1960 1965
Met Leu Ile Val Lys Tyr His Ala Gln Asp Asp Ile Asp Phe Lys Leu
1970 1975 1980
Asp Asn Ile Thr Ile Leu Lys Thr Tyr Val Cys Leu Gly Ser Lys Leu
1985 1990 1995 2000
Lys Gly Ser Glu Val Tyr Leu Val Leu Thr Ile Gly Pro Ala Asn Ile
2005 2010 2015
Phe Pro Val Phe Asn Val Val Gln Asn Ala Lys Leu Ile Leu Ser Arg
2020 2025 2030
Thr Lys Asn Phe Ile Met Pro Lys Lys Ala Asp Lys Glu Ser Ile Asp
2035 2040 2045
Ala Asn Ile Lys Ser Leu Ile Pro Phe Leu Cys Tyr Pro Ile Thr Lys
2050 2055 2060

Lys Gly Ile Asn Thr Ala Leu Ser Lys Leu Lys Ser Val Val Ser Gly
2065 2070 2075 2080
Asp Ile Leu Ser Tyr Ser Ile Ala Gly Arg Asn Glu Val Phe Ser Asn
2085 2090 2095
Lys Leu Ile Asn His Lys His Met Asn Ile Leu Lys Trp Phe Asn His
2100 2105 2110
Val Leu Asn Phe Arg Ser Thr Glu Leu Asn Tyr Asn His Leu Tyr Met
2115 2120 2125
Val Glu Ser Thr Tyr Pro Tyr Leu Ser Glu Leu Leu Asn Ser Leu Thr
2130 2135 2140
Thr Asn Glu Leu Lys Lys Leu Ile Lys Ile Thr Gly Ser Leu Leu Tyr
2145 2150 2155 2160
Asn Phe His Asn Glu
2165

<210> 394
<211> 241
<212> PRT
<213> Human respiratory syncytial virus

<220>
<223> phosphoprotein P of Human respiratory syncytial virus

<400> 394
Met Glu Lys Phe Ala Pro Glu Phe His Gly Glu Asp Ala Asn Asn Arg
1 5 10 15
Ala Thr Lys Phe Leu Glu Ser Ile Lys Gly Lys Phe Thr Ser Pro Lys
20 25 30
Asp Pro Lys Lys Lys Asp Ser Ile Ile Ser Val Asn Ser Ile Asp Ile
35 40 45
Glu Val Thr Lys Glu Ser Pro Ile Thr Ser Asn Ser Thr Ile Met Asn
50 55 60
Pro Thr Asn Glu Thr Asp Asp Thr Val Gly Asn Lys Pro Asn Tyr Gln
65 70 75 80
Arg Lys Pro Leu Val Ser Phe Lys Glu Asp Pro Met Leu Ser Asp Asn
85 90 95
Pro Phe Ser Lys Leu Tyr Lys Glu Thr Ile Glu Thr Phe Asp Asn Asn
100 105 110
Glu Glu Glu Ser Ser Tyr Ser Tyr Glu Glu Ile Asn Asp Gln Thr Asn
115 120 125
Asp Asn Ile Thr Ala Arg Leu Asp Arg Ile Asp Glu Lys Leu Ser Glu
130 135 140
Ile Leu Gly Met Leu His Thr Leu Val Val Ala Ser Ala Gly Pro Thr
145 150 155 160
Ser Ala Arg Asp Gly Ile Arg Asp Ala Met Val Gly Leu Arg Glu Glu
165 170 175
Met Ile Glu Lys Ile Arg Thr Glu Ala Leu Met Thr Asn Asn Arg Leu
180 185 190
Glu Ala Met Ala Arg Leu Arg Asn Glu Glu Ser Glu Lys Met Ala Lys
195 200 205
Asp Thr Ser Asp Glu Val Ser Leu Asn Pro Thr Ser Glu Lys Leu Asn
210 215 220
Asn Leu Leu Glu Gly Asn Asp Ser Asp Asp Asp Leu Ser Leu Glu Asp
225 230 235 240
Phe

<210> 395
<211> 83
<212> PRT
<213> Human respiratory syncytial virus

<220>
<223> attachment glycoprotein G of Human respiratory syncytial virus

<400> 395
Lys Arg Asp Pro Lys Thr Pro Ala Lys Met Leu Asn Lys Glu Thr Thr
1 5 10 15
Thr Asn Pro Thr Lys Asn Leu Thr Leu Lys Thr Thr Glu Arg Asp Thr
20 25 30
Ser Thr Ser Gln Ser Thr Val Leu Asp Thr Ser Thr Ser Lys His Ile
35 40 45
Ile Leu Gln Gln Ser Leu His Ser Thr Thr Pro Glu Asn Thr Pro Asn
50 55 60
Phe Thr Gln Thr Pro Thr Ala Ser Glu Pro Ser Thr Ser Asn Ser Thr
65 70 75 80
Gln Lys Thr

<210> 396
<211> 391
<212> PRT
<213> human respiratory syncytial virus (strain 18537)

<220>
<223> nucleocapsid protein of Human respiratory syncytial virus

<400> 396
Met Ala Leu Ser Lys Val Lys Leu Asn Asp Thr Leu Asn Lys Asp Gln
1 5 10 15
Leu Leu Ser Ser Ser Lys Tyr Thr Ile Gln Arg Ser Thr Gly Asp Asn
20 25 30
Ile Asp Thr Pro Asn Tyr Asp Val Gln Lys His Leu Asn Lys Leu Cys
35 40 45
Gly Met Leu Leu Ile Thr Glu Asp Ala Asn His Lys Phe Thr Gly Leu
50 55 60
Ile Gly Met Leu Tyr Ala Met Ser Arg Leu Gly Arg Glu Asp Thr Ile
65 70 75 80
Lys Ile Leu Lys Asp Ala Gly Tyr His Val Lys Ala Asn Gly Val Asp
85 90 95
Ile Thr Thr Tyr Arg Gln Asp Ile Asn Gly Lys Glu Met Lys Phe Glu
100 105 110
Val Leu Thr Leu Ser Ser Leu Thr Ser Glu Ile Gln Val Asn Ile Glu
115 120 125
Ile Glu Ser Arg Lys Ser Tyr Lys Lys Leu Leu Lys Glu Met Gly Glu
130 135 140
Val Ala Pro Glu Tyr Arg His Asp Ser Pro Asp Cys Gly Met Ile Ile
145 150 155 160
Leu Cys Ile Ala Ala Leu Val Ile Thr Lys Leu Ala Ala Gly Asp Arg
165 170 175
Ser Gly Leu Thr Ala Val Ile Arg Arg Ala Asn Asn Val Leu Lys Asn
180 185 190
Glu Ile Lys Arg Tyr Lys Gly Leu Ile Pro Lys Asp Ile Ala Asn Ser
195 200 205
Phe Tyr Glu Val Phe Glu Lys His Pro His Leu Ile Asp Val Phe Val
210 215 220
His Phe Gly Ile Ala Gln Ser Ser Thr Arg Gly Gly Ser Arg Val Glu
225 230 235 240
Gly Ile Phe Ala Gly Leu Phe Met Asn Ala Tyr Gly Ser Gly Gln Val
245 250 255
Met Leu Arg Trp Gly Val Leu Ala Lys Ser Val Lys Asn Ile Met Leu

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            260                 265                 270
Gly His Ala Ser Val Gln Ala Glu Met Glu Gln Val Val Glu Val Tyr
        275                 280                 285
Glu Tyr Ala Gln Lys Leu Gly Gly Glu Ala Gly Phe Tyr His Ile Leu
    290                 295                 300
Asn Asn Pro Lys Ala Ser Leu Leu Ser Leu Thr Gln Phe Pro Asn Phe
305                 310                 315                 320
Ser Ser Val Val Leu Gly Asn Ala Ala Gly Leu Gly Ile Met Gly Glu
                325                 330                 335
Tyr Arg Gly Thr Pro Arg Asn Gln Asp Leu Tyr Asp Ala Ala Lys Ala
            340                 345                 350
Tyr Ala Glu Gln Leu Lys Glu Asn Gly Val Ile Asn Tyr Ser Val Leu
        355                 360                 365
Asp Leu Thr Ala Glu Glu Leu Glu Ala Ile Lys His Gln Leu Asn Pro
    370                 375                 380
Lys Glu Asp Asp Val Glu Leu
385                 390


<210> 397
<211> 391
<212> PRT
<213> Human respiratory syncytial virus

<220>
<223>  nucleoprotein (N)  of Human respiratory syncytial virus

<400> 397
Met Ala Leu Ser Lys Val Lys Leu Asn Asp Thr Leu Asn Lys Asp Gln
 1               5                  10                  15
Leu Leu Ser Ser Ser Lys Tyr Thr Ile Gln Arg Ser Thr Gly Asp Ser
            20                  25                  30
Ile Asp Thr Pro Asn Tyr Asp Val Gln Lys His Ile Asn Lys Leu Cys
        35                  40                  45
Gly Met Leu Leu Ile Thr Glu Asp Ala Asn His Lys Phe Thr Gly Leu
    50                  55                  60
Ile Gly Met Leu Tyr Ala Met Ser Arg Leu Gly Arg Glu Asp Thr Ile
65                  70                  75                  80
Lys Ile Leu Arg Asp Ala Gly Tyr His Val Lys Ala Asn Gly Val Asp
                85                  90                  95
Val Thr Thr His Arg Gln Asp Ile Asn Gly Lys Glu Met Lys Phe Glu
            100                 105                 110
Val Leu Thr Leu Ser Ser Leu Thr Thr Glu Ile Gln Ile Asn Ile Glu
        115                 120                 125
Ile Glu Ser Arg Lys Ser Tyr Lys Lys Met Leu Lys Glu Met Gly Glu
    130                 135                 140
Val Ala Pro Glu Tyr Arg His Asp Ser Pro Asp Cys Gly Met Ile Ile
145                 150                 155                 160
Leu Cys Ile Ala Ala Leu Val Ile Thr Lys Leu Ala Ala Gly Asp Arg
                165                 170                 175
Ser Gly Leu Thr Ala Val Ile Arg Arg Ala Asn Asn Val Leu Lys Asn
            180                 185                 190
Glu Met Lys Arg Tyr Lys Gly Leu Leu Pro Lys Asp Ile Ala Asn Ser
        195                 200                 205
Phe Tyr Glu Val Phe Glu Lys Tyr Pro His Phe Ile Asp Val Phe Val
    210                 215                 220
His Phe Gly Ile Ala Gln Ser Ser Thr Arg Gly Gly Ser Arg Val Glu
225                 230                 235                 240
Gly Ile Phe Ala Gly Leu Phe Met Asn Ala Tyr Gly Ala Gly Gln Val
                245                 250                 255
Met Leu Arg Trp Gly Val Leu Ala Lys Ser Val Lys Asn Ile Met Leu
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260 265 270
Gly His Ala Ser Val Gln Ala Glu Met Glu Gln Val Val Glu Val Tyr
275 280 285
Glu Tyr Ala Gln Lys Leu Gly Gly Glu Ala Gly Phe Tyr His Ile Leu
290 295 300
Asn Asn Pro Lys Ala Ser Leu Leu Ser Leu Thr Gln Phe Pro His Phe
305 310 315 320
Ser Ser Val Val Leu Gly Asn Ala Ala Gly Leu Gly Ile Met Gly Glu
325 330 335
Tyr Arg Gly Thr Pro Arg Asn Gln Asp Leu Tyr Asp Ala Ala Lys Ala
340 345 350
Tyr Ala Glu Gln Leu Lys Glu Asn Gly Val Ile Asn Tyr Ser Val Leu
355 360 365
Asp Leu Thr Ala Glu Glu Leu Glu Ala Ile Lys His Gln Leu Asn Pro
370 375 380
Lys Asp Asn Asp Val Glu Leu
385 390

<210> 398
<211> 256
<212> PRT
<213> Human respiratory syncytial virus

<220>
<223>matrix protein of Human respiratory syncytial virus

<400> 398
Met Glu Thr Tyr Val Asn Lys Leu His Glu Gly Ser Thr Tyr Thr Ala
1 5 10 15
Ala Val Gln Tyr Asn Val Leu Glu Lys Asp Asp Asp Pro Ala Ser Leu
20 25 30
Thr Ile Trp Val Pro Met Phe Gln Ser Ser Met Pro Ala Asp Leu Leu
35 40 45
Ile Lys Glu Leu Ala Asn Val Asn Ile Leu Val Lys Gln Ile Ser Thr
50 55 60
Pro Lys Gly Pro Ser Leu Arg Val Met Ile Asn Ser Arg Ser Ala Val
65 70 75 80
Leu Ala Gln Met Pro Ser Lys Phe Thr Ile Cys Ala Asn Val Ser Leu
85 90 95
Asp Glu Arg Ser Lys Leu Ala Tyr Asp Val Thr Thr Pro Cys Glu Ile
100 105 110
Lys Ala Cys Ser Leu Thr Cys Leu Lys Ser Lys Asn Met Leu Thr Thr
115 120 125
Val Lys Asp Leu Thr Met Lys Thr Leu Asn Pro Thr His Asp Ile Ile
130 135 140
Ala Leu Cys Glu Phe Glu Asn Ile Val Thr Ser Lys Lys Val Ile Ile
145 150 155 160
Pro Thr Tyr Leu Arg Ser Ile Ser Val Arg Asn Lys Asp Leu Asn Thr
165 170 175
Leu Glu Asn Ile Thr Thr Thr Glu Phe Lys Asn Ala Ile Thr Asn Ala
180 185 190
Lys Ile Ile Pro Tyr Ser Gly Leu Leu Leu Val Ile Thr Val Thr Asp
195 200 205
Asn Lys Gly Ala Phe Lys Tyr Ile Lys Pro Gln Ser Gln Phe Ile Val
210 215 220
Asp Leu Gly Ala Tyr Leu Glu Lys Glu Ser Ile Tyr Tyr Val Thr Thr
225 230 235 240
Asn Trp Lys His Thr Ala Thr Arg Phe Ala Ile Lys Pro Met Glu Asp
245 250 255

<210> 399
<211> 1185
<212> DNA
<213> Human metapneumovirus

<220>
<221> CDS
<222> (1)...(1185)
<223> Nucleoprotein (N)

<400> 399
atg tct ctt caa ggg att cac ctg agt gat tta tca tac aag cat gct 48
Met Ser Leu Gln Gly Ile His Leu Ser Asp Leu Ser Tyr Lys His Ala
1 5 10 15
ata tta aaa gag tct cag tac aca ata aaa aga gat gtg ggt aca aca 96
Ile Leu Lys Glu Ser Gln Tyr Thr Ile Lys Arg Asp Val Gly Thr Thr
20 25 30
act gca gtg aca ccc tca tca ttg caa caa gaa ata aca ctg ttg tgt 144
Thr Ala Val Thr Pro Ser Ser Leu Gln Gln Glu Ile Thr Leu Leu Cys
35 40 45
gga gaa att ctg tat gct aaa cat gct gac tac aaa tat gct gca gaa 192
Gly Glu Ile Leu Tyr Ala Lys His Ala Asp Tyr Lys Tyr Ala Ala Glu
50 55 60
ata gga ata caa tat att agc aca gct tta gga tca gag aga gtg cag 240
Ile Gly Ile Gln Tyr Ile Ser Thr Ala Leu Gly Ser Glu Arg Val Gln
65 70 75 80
cag att ctg agg aac tca ggc agt gaa gtc caa gtg gtc tta acc aga 288
Gln Ile Leu Arg Asn Ser Gly Ser Glu Val Gln Val Val Leu Thr Arg
85 90 95
acg tac tct ctg ggg aaa att aaa aac aat aaa gga gaa gat tta cag 336
Thr Tyr Ser Leu Gly Lys Ile Lys Asn Asn Lys Gly Glu Asp Leu Gln
100 105 110
atg tta gac ata cac ggg gta gag aag agc tgg gta gaa gag ata gac 384
Met Leu Asp Ile His Gly Val Glu Lys Ser Trp Val Glu Glu Ile Asp
115 120 125
aaa gaa gca agg aaa aca atg gca acc ttg ctt aag gaa tca tca ggt 432
Lys Glu Ala Arg Lys Thr Met Ala Thr Leu Leu Lys Glu Ser Ser Gly
130 135 140
aat atc cca caa aat cag agg ccc tca gca cca gac aca ccc ata atc 480
Asn Ile Pro Gln Asn Gln Arg Pro Ser Ala Pro Asp Thr Pro Ile Ile
145 150 155 160
tta tta tgt gta ggt gcc tta ata ttc act aaa cta gca tca acc ata 528
Leu Leu Cys Val Gly Ala Leu Ile Phe Thr Lys Leu Ala Ser Thr Ile
165 170 175
gaa gtg gga cta gag acc aca gtc aga agg gct aac cgt gta cta agt 576
Glu Val Gly Leu Glu Thr Thr Val Arg Arg Ala Asn Arg Val Leu Ser
180 185 190
gat gca ctc aag aga tac cct aga atg gac ata cca aag att gcc aga 624
Asp Ala Leu Lys Arg Tyr Pro Arg Met Asp Ile Pro Lys Ile Ala Arg
195 200 205
tcc ttc tat gac tta ttt gaa caa aaa gtg tat cac aga agt ttg ttc 672
Ser Phe Tyr Asp Leu Phe Glu Gln Lys Val Tyr His Arg Ser Leu Phe
210 215 220
att gag tat ggc aaa gca tta ggc tca tca tct aca ggc agc aaa gca 720
Ile Glu Tyr Gly Lys Ala Leu Gly Ser Ser Ser Thr Gly Ser Lys Ala
225 230 235 240
gaa agt cta ttt gtt aat ata ttc atg caa gct tat ggg gcc ggt caa 768
Glu Ser Leu Phe Val Asn Ile Phe Met Gln Ala Tyr Gly Ala Gly Gln
245 250 255
aca atg cta agg tgg ggg gtc att gcc agg tca tcc aac aat ata atg 816

Thr Met Leu Arg Trp Gly Val Ile Ala Arg Ser Ser Asn Asn Ile Met
260 265 270
tta gga cat gta tcc gtc caa gct gag tta aaa cag gtc aca gaa gtc 864
Leu Gly His Val Ser Val Gln Ala Glu Leu Lys Gln Val Thr Glu Val
275 280 285
tat gac ttg gtg cga gaa atg ggc cct gaa tct gga ctt cta cat tta 912
Tyr Asp Leu Val Arg Glu Met Gly Pro Glu Ser Gly Leu Leu His Leu
290 295 300
agg caa agc cca aaa gct gga ctg tta tca cta gcc aac tgt ccc aac 960
Arg Gln Ser Pro Lys Ala Gly Leu Leu Ser Leu Ala Asn Cys Pro Asn
305 310 315 320
ttt gca agt gtt gtt ctc gga aat gcc tca ggc tta ggc ata atc ggt 1008
Phe Ala Ser Val Val Leu Gly Asn Ala Ser Gly Leu Gly Ile Ile Gly
325 330 335
atg tat cga ggg aga gta cca aac aca gaa tta ttt tca gca gct gaa 1056
Met Tyr Arg Gly Arg Val Pro Asn Thr Glu Leu Phe Ser Ala Ala Glu
340 345 350
agt tat gcc aaa agt ttg aaa gaa agc aat aaa ata aat ttc tct tca 1104
Ser Tyr Ala Lys Ser Leu Lys Glu Ser Asn Lys Ile Asn Phe Ser Ser
355 360 365
tta gga ctt aca gat gaa gag aaa gag gct gca gaa cat ttc tta aat 1152
Leu Gly Leu Thr Asp Glu Glu Lys Glu Ala Ala Glu His Phe Leu Asn
370 375 380
gtg agt gac gac agt caa aat gat tat gag taa 1185
Val Ser Asp Asp Ser Gln Asn Asp Tyr Glu *
385 390

<210> 400
<211> 885
<212> DNA
<213> Human metapneumovirus

<220>
<221> CDS
<222> (1)...(885)
<223> Phosphoprotein (P)

<400> 400
atg tca ttc cct gaa gga aaa gat att ctt ttc atg ggt aat gaa gca 48
Met Ser Phe Pro Glu Gly Lys Asp Ile Leu Phe Met Gly Asn Glu Ala
1 5 10 15
gca aaa tta gca gaa gct ttc cag aaa tca tta aga aaa cca ggt cat 96
Ala Lys Leu Ala Glu Ala Phe Gln Lys Ser Leu Arg Lys Pro Gly His
20 25 30
aaa aga tct caa tct att ata gga gaa aaa gtg aat act gta tca gaa 144
Lys Arg Ser Gln Ser Ile Ile Gly Glu Lys Val Asn Thr Val Ser Glu
35 40 45
aca ttg gaa tta cct act atc agt aga cct gca aaa cca acc ata ccg 192
Thr Leu Glu Leu Pro Thr Ile Ser Arg Pro Ala Lys Pro Thr Ile Pro
50 55 60
tca gaa cca aag tta gca tgg aca gat aaa ggt ggg gca acc aaa act 240
Ser Glu Pro Lys Leu Ala Trp Thr Asp Lys Gly Gly Ala Thr Lys Thr
65 70 75 80
gaa ata aag caa gca atc aaa gtc atg gat ccc att gaa gaa gaa gag 288
Glu Ile Lys Gln Ala Ile Lys Val Met Asp Pro Ile Glu Glu Glu Glu
85 90 95
tct acc gag aag aag gtg cta ccc tcc agt gat ggg aaa acc cct gca 336
Ser Thr Glu Lys Lys Val Leu Pro Ser Ser Asp Gly Lys Thr Pro Ala
100 105 110
gaa aag aaa ctg aaa cca tca act aac acc aaa aag aag gtt tca ttt 384
Glu Lys Lys Leu Lys Pro Ser Thr Asn Thr Lys Lys Lys Val Ser Phe

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        115                 120                 125
aca cca aat gaa cca ggg aaa tat aca aag ttg gaa aaa gat gct cta     432
Thr Pro Asn Glu Pro Gly Lys Tyr Thr Lys Leu Glu Lys Asp Ala Leu
    130                 135                 140
gat ttg ctc tca gat aat gaa gaa gaa gat gca gaa tct tca atc tta     480
Asp Leu Leu Ser Asp Asn Glu Glu Glu Asp Ala Glu Ser Ser Ile Leu
145                 150                 155                 160
acc ttt gaa gaa aga gat act tca tca tta agc att gag gcc aga ttg     528
Thr Phe Glu Glu Arg Asp Thr Ser Ser Leu Ser Ile Glu Ala Arg Leu
                165                 170                 175
gaa tca ata gag gag aaa tta agc atg ata tta ggg cta tta aga aca     576
Glu Ser Ile Glu Glu Lys Leu Ser Met Ile Leu Gly Leu Leu Arg Thr
            180                 185                 190
ctc aac att gct aca gca gga ccc aca gca gca aga gat ggg atc aga     624
Leu Asn Ile Ala Thr Ala Gly Pro Thr Ala Ala Arg Asp Gly Ile Arg
        195                 200                 205
gat gca atg att ggc gta aga gag gaa tta ata gca gac ata ata aag     672
Asp Ala Met Ile Gly Val Arg Glu Glu Leu Ile Ala Asp Ile Ile Lys
    210                 215                 220
gaa gct aaa ggg aaa gca gca gaa atg atg gaa gag gaa atg agt caa     720
Glu Ala Lys Gly Lys Ala Ala Glu Met Met Glu Glu Glu Met Ser Gln
225                 230                 235                 240
cga tca aaa ata gga aat ggt agt gta aaa tta aca gaa aaa gca aaa     768
Arg Ser Lys Ile Gly Asn Gly Ser Val Lys Leu Thr Glu Lys Ala Lys
                245                 250                 255
gag ctc aac aaa att gtt gaa gat gaa agc aca agt gga gaa tcc gaa     816
Glu Leu Asn Lys Ile Val Glu Asp Glu Ser Thr Ser Gly Glu Ser Glu
            260                 265                 270
gaa gaa gaa gaa cca aaa gac aca caa gac aat agt caa gaa gat gac     864
Glu Glu Glu Glu Pro Lys Asp Thr Gln Asp Asn Ser Gln Glu Asp Asp
        275                 280                 285
att tac cag tta att atg tag                                         885
Ile Tyr Gln Leu Ile Met  *
    290


<210> 401
<211> 765
<212> DNA
<213> Human metapneumovirus

<220>
<221> CDS
<222> (1)...(765)
<223> Matrix Protein (M)

<400> 401
atg gag tcc tac cta gta gac acc tat caa ggc att cct tac aca gca     48
Met Glu Ser Tyr Leu Val Asp Thr Tyr Gln Gly Ile Pro Tyr Thr Ala
 1               5                  10                  15
gct gtt caa gtt gat cta ata gaa aag gac ctg tta cct gca agc cta     96
Ala Val Gln Val Asp Leu Ile Glu Lys Asp Leu Leu Pro Ala Ser Leu
            20                  25                  30
aca ata tgg ttc cct ttg ttt cag gcc aac aca cca cca gca gtg ctg     144
Thr Ile Trp Phe Pro Leu Phe Gln Ala Asn Thr Pro Pro Ala Val Leu
        35                  40                  45
ctc gat cag cta aaa acc ctg aca ata acc act ctg tat gct gca tca     192
Leu Asp Gln Leu Lys Thr Leu Thr Ile Thr Thr Leu Tyr Ala Ala Ser
    50                  55                  60
caa aat ggt cca ata ctc aaa gtg aat gca tca gcc caa ggt gca gca     240
Gln Asn Gly Pro Ile Leu Lys Val Asn Ala Ser Ala Gln Gly Ala Ala
```

65 70 75 80
atg tct gta ctt ccc aaa aaa ttt gaa gtc aat gcg act gta gca ctc 288
Met Ser Val Leu Pro Lys Lys Phe Glu Val Asn Ala Thr Val Ala Leu
85 90 95
gat gaa tat agc aaa ctg gaa ttt gac aaa ctc aca gtc tgt gaa gta 336
Asp Glu Tyr Ser Lys Leu Glu Phe Asp Lys Leu Thr Val Cys Glu Val
100 105 110
aaa aca gtt tac tta aca acc atg aaa cca tac ggg atg gta tca aaa 384
Lys Thr Val Tyr Leu Thr Thr Met Lys Pro Tyr Gly Met Val Ser Lys
115 120 125
ttt gtg agc tca gcc aaa tca gtt ggc aaa aaa aca cat gat cta atc 432
Phe Val Ser Ser Ala Lys Ser Val Gly Lys Lys Thr His Asp Leu Ile
130 135 140
gca cta tgt gat ttt atg gat cta gaa aag aac aca cct gtt aca ata 480
Ala Leu Cys Asp Phe Met Asp Leu Glu Lys Asn Thr Pro Val Thr Ile
145 150 155 160
cca gca ttc atc aaa tca gtt tca atc aaa gag agt gag tca gct act 528
Pro Ala Phe Ile Lys Ser Val Ser Ile Lys Glu Ser Glu Ser Ala Thr
165 170 175
gtt gaa gct gct ata agc agt gaa gca gac caa gct cta aca cag gcc 576
Val Glu Ala Ala Ile Ser Ser Glu Ala Asp Gln Ala Leu Thr Gln Ala
180 185 190
aaa att gca cct tat gcg gga tta att atg atc atg act atg aac aat 624
Lys Ile Ala Pro Tyr Ala Gly Leu Ile Met Ile Met Thr Met Asn Asn
195 200 205
ccc aaa ggc ata ttc aaa aag ctt gga gct ggg act caa gtc ata gta 672
Pro Lys Gly Ile Phe Lys Lys Leu Gly Ala Gly Thr Gln Val Ile Val
210 215 220
gaa cta gga gca tat gtc cag gct gaa agc ata agc aaa ata tgc aag 720
Glu Leu Gly Ala Tyr Val Gln Ala Glu Ser Ile Ser Lys Ile Cys Lys
225 230 235 240
act tgg agc cat caa ggg aca aga tat gtc ttg aag tcc aga taa 765
Thr Trp Ser His Gln Gly Thr Arg Tyr Val Leu Lys Ser Arg *
245 250

<210> 402
<211> 564
<212> DNA
<213> Human metapneumovirus

<220>
<221> CDS
<222> (1)...(564)
<223> Matrix Protein 2-1 (M2)

<400> 402
atg tct cgc aag gct ccg tgc aaa tat gaa gtg cgg ggc aaa tgc aat 48
Met Ser Arg Lys Ala Pro Cys Lys Tyr Glu Val Arg Gly Lys Cys Asn
1 5 10 15
aga gga agt gag tgc aag ttt aac cac aat tac tgg agt tgg cca gat 96
Arg Gly Ser Glu Cys Lys Phe Asn His Asn Tyr Trp Ser Trp Pro Asp
20 25 30
aga tac tta tta ata aga tca aat tat tta tta aat caa ctt tta agg 144
Arg Tyr Leu Leu Ile Arg Ser Asn Tyr Leu Leu Asn Gln Leu Leu Arg
35 40 45
aac act gat aga gct gat ggc tta tca ata ata tca gga gca ggc aga 192
Asn Thr Asp Arg Ala Asp Gly Leu Ser Ile Ile Ser Gly Ala Gly Arg
50 55 60
gaa gat agg aca caa gat ttt gtc cta ggt tcc acc aat gtg gtt caa 240
Glu Asp Arg Thr Gln Asp Phe Val Leu Gly Ser Thr Asn Val Val Gln
65 70 75 80

ggt tat att gat gat aac caa agc ata aca aaa gct gca gcc tgt tac 288
Gly Tyr Ile Asp Asp Asn Gln Ser Ile Thr Lys Ala Ala Ala Cys Tyr
85 90 95
agt cta cat aat ata atc aaa caa cta caa gaa gtt gaa gtt agg cag 336
Ser Leu His Asn Ile Ile Lys Gln Leu Gln Glu Val Glu Val Arg Gln
100 105 110
gct aga gat aac aaa cta tct gac agc aaa cat gta gca ctt cac aac 384
Ala Arg Asp Asn Lys Leu Ser Asp Ser Lys His Val Ala Leu His Asn
115 120 125
tta gtc cta tct tat atg gag atg agc aaa act cct gca tct tta atc 432
Leu Val Leu Ser Tyr Met Glu Met Ser Lys Thr Pro Ala Ser Leu Ile
130 135 140
aac aat ctc aag aga ctg ccg aga gag aaa ctg aaa aaa tta gca aag 480
Asn Asn Leu Lys Arg Leu Pro Arg Glu Lys Leu Lys Lys Leu Ala Lys
145 150 155 160
ctc ata att gac tta tca gca ggt gct gaa aat gac tct tca tat gcc 528
Leu Ile Ile Asp Leu Ser Ala Gly Ala Glu Asn Asp Ser Ser Tyr Ala
165 170 175
ttg caa gac agt gaa agc act aat caa gtg cag tga 564
Leu Gln Asp Ser Glu Ser Thr Asn Gln Val Gln *
180 185

<210> 403
<211> 216
<212> DNA
<213> Human metapneumovirus

<220>
<221> CDS
<222> (1)...(216)
<223> Matrix Protein 2-2 (M2)

<400> 403
atg act ctt cat atg cct tgc aag aca gtg aaa gca cta atc aag tgc 48
Met Thr Leu His Met Pro Cys Lys Thr Val Lys Ala Leu Ile Lys Cys
1 5 10 15
agt gag cat ggt cca gtt ttc att act ata gag gtt gat gac atg ata 96
Ser Glu His Gly Pro Val Phe Ile Thr Ile Glu Val Asp Asp Met Ile
20 25 30
tgg act cac aag gac tta aaa gaa gct tta tct gat ggg ata gtg aag 144
Trp Thr His Lys Asp Leu Lys Glu Ala Leu Ser Asp Gly Ile Val Lys
35 40 45
tct cat act aac att tac aat tgt tat tta gaa aac ata gaa att ata 192
Ser His Thr Asn Ile Tyr Asn Cys Tyr Leu Glu Asn Ile Glu Ile Ile
50 55 60
tat gtc aag gct tac tta agt tag 216
Tyr Val Lys Ala Tyr Leu Ser *
65 70

<210> 404
<211> 552
<212> DNA
<213> Human metapneumovirus

<220>
<221> CDS
<222> (1)...(552)
<223> Small Hydrophobic Protein (SH)

<400> 404

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atg ata aca tta gat gtc att aaa agt gat ggg tct tca aaa aca tgt      48
Met Ile Thr Leu Asp Val Ile Lys Ser Asp Gly Ser Ser Lys Thr Cys
 1               5                  10                  15
act cac ctc aaa aaa ata att aaa gac cac tct ggt aaa gtg ctt att      96
Thr His Leu Lys Lys Ile Ile Lys Asp His Ser Gly Lys Val Leu Ile
            20                  25                  30
gta ctt aag tta ata tta gct tta cta aca ttt ctc aca gta aca atc     144
Val Leu Lys Leu Ile Leu Ala Leu Leu Thr Phe Leu Thr Val Thr Ile
        35                  40                  45
acc atc aat tat ata aaa gtg gaa aac aat ctg caa ata tgc cag tca     192
Thr Ile Asn Tyr Ile Lys Val Glu Asn Asn Leu Gln Ile Cys Gln Ser
    50                  55                  60
aaa act gaa tca gac aaa aag gac tca tca tca aat acc aca tca gtc     240
Lys Thr Glu Ser Asp Lys Lys Asp Ser Ser Ser Asn Thr Thr Ser Val
65                  70                  75                  80
aca acc aag act act cta aat cat gat atc aca cag tat ttt aaa agt     288
Thr Thr Lys Thr Thr Leu Asn His Asp Ile Thr Gln Tyr Phe Lys Ser
                85                  90                  95
ttg att caa agg tat aca aac tct gca ata aac agt gac aca tgc tgg     336
Leu Ile Gln Arg Tyr Thr Asn Ser Ala Ile Asn Ser Asp Thr Cys Trp
            100                 105                 110
aaa ata aac aga aat caa tgc aca aat ata aca aca tac aaa ttt tta     384
Lys Ile Asn Arg Asn Gln Cys Thr Asn Ile Thr Thr Tyr Lys Phe Leu
        115                 120                 125
tgt ttt aaa tct gaa gac aca aaa acc aac aat tgt gat aaa ctg aca     432
Cys Phe Lys Ser Glu Asp Thr Lys Thr Asn Asn Cys Asp Lys Leu Thr
    130                 135                 140
gat tta tgc aga aac aaa cca aaa cca gca gtt gga gtg tat cac ata     480
Asp Leu Cys Arg Asn Lys Pro Lys Pro Ala Val Gly Val Tyr His Ile
145                 150                 155                 160
gta gaa tgc cat tgt ata tac aca gtt aaa tgg aag tgc tat cat tac     528
Val Glu Cys His Cys Ile Tyr Thr Val Lys Trp Lys Cys Tyr His Tyr
                165                 170                 175
cca acc gat gaa acc caa tcc taa                                     552
Pro Thr Asp Glu Thr Gln Ser  *
            180
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<210> 405
<211> 2005
<212> PRT
<213> Human metapneumovirus

<220>
<223> RNA-dependent RNA polymerase (L) of Human metapneumovirus

<400> 405

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Met Asp Pro Leu Asn Glu Ser Thr Val Asn Val Tyr Leu Pro Asp Ser
 1               5                  10                  15
Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Thr Asn Ala Ile Gly Ser
            20                  25                  30
Cys Leu Leu Lys Arg Pro Tyr Leu Lys Asn Asp Asn Thr Ala Lys Val
        35                  40                  45
Ala Ile Glu Asn Pro Val Ile Glu His Val Arg Leu Lys Asn Ala Val
    50                  55                  60
Asn Ser Lys Met Lys Ile Ser Asp Tyr Lys Ile Val Glu Pro Val Asn
65                  70                  75                  80
Met Gln His Glu Ile Met Lys Asn Val His Ser Cys Glu Leu Thr Leu
                85                  90                  95
Leu Lys Gln Phe Leu Thr Arg Ser Lys Asn Ile Ser Thr Leu Lys Leu
            100                 105                 110
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Asn Met Ile Cys Asp Trp Leu Gln Leu Lys Ser Thr Ser Asp Asp Thr
115 120 125
Ser Ile Leu Ser Phe Ile Asp Val Glu Phe Ile Pro Ser Trp Val Ser
130 135 140
Asn Trp Phe Ser Asn Trp Tyr Asn Leu Asn Lys Leu Ile Leu Glu Phe
145 150 155 160
Arg Lys Glu Glu Val Ile Arg Thr Gly Ser Ile Leu Cys Arg Ser Leu
165 170 175
Gly Lys Leu Val Phe Val Val Ser Ser Tyr Gly Cys Ile Val Lys Ser
180 185 190
Asn Lys Ser Lys Arg Val Ser Phe Phe Thr Tyr Asn Gln Leu Leu Thr
195 200 205
Trp Lys Asp Val Met Leu Ser Arg Phe Asn Ala Asn Phe Cys Ile Trp
210 215 220
Val Ser Asn Ser Leu Asn Glu Asn Gln Glu Gly Leu Gly Leu Arg Ser
225 230 235 240
Asn Leu Gln Gly Ile Leu Thr Asn Lys Leu Tyr Glu Thr Val Asp Tyr
245 250 255
Met Leu Ser Leu Cys Cys Asn Glu Gly Phe Ser Leu Val Lys Glu Phe
260 265 270
Glu Gly Phe Ile Met Ser Glu Ile Leu Arg Ile Thr Glu His Ala Gln
275 280 285
Phe Ser Thr Arg Phe Arg Asn Thr Leu Leu Asn Gly Leu Thr Asp Gln
290 295 300
Leu Thr Lys Leu Lys Asn Lys Asn Arg Leu Arg Val His Gly Thr Val
305 310 315 320
Leu Glu Asn Asn Asp Tyr Pro Met Tyr Glu Val Val Leu Lys Leu Leu
325 330 335
Gly Asp Thr Leu Arg Cys Ile Lys Leu Leu Ile Asn Lys Asn Leu Glu
340 345 350
Asn Ala Ala Glu Leu Tyr Tyr Ile Phe Arg Ile Phe Gly His Pro Met
355 360 365
Val Asp Glu Arg Asp Ala Met Asp Ala Val Lys Leu Asn Asn Glu Ile
370 375 380
Thr Lys Ile Leu Arg Trp Glu Ser Leu Thr Glu Leu Arg Gly Ala Phe
385 390 395 400
Ile Leu Arg Ile Ile Lys Gly Phe Val Asp Asn Asn Lys Arg Trp Pro
405 410 415
Lys Ile Lys Asn Leu Lys Val Leu Ser Lys Arg Trp Thr Met Tyr Phe
420 425 430
Lys Ala Lys Ser Tyr Pro Ser Gln Leu Glu Leu Ser Glu Gln Asp Phe
435 440 445
Leu Glu Leu Ala Ala Ile Gln Phe Glu Gln Glu Phe Ser Val Pro Glu
450 455 460
Lys Thr Asn Leu Glu Met Val Leu Asn Asp Lys Ala Ile Ser Pro Pro
465 470 475 480
Lys Arg Leu Ile Trp Ser Val Tyr Pro Lys Asn Tyr Leu Pro Glu Lys
485 490 495
Ile Lys Asn Arg Tyr Leu Glu Glu Thr Phe Asn Ala Ser Asp Ser Leu
500 505 510
Lys Thr Arg Arg Val Leu Glu Tyr Tyr Leu Lys Asp Asn Lys Phe Asp
515 520 525
Gln Lys Glu Leu Lys Ser Tyr Val Val Lys Gln Glu Tyr Leu Asn Asp
530 535 540
Lys Asp His Ile Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser Val
545 550 555 560
Gly Arg Met Phe Ala Met Gln Pro Gly Lys Gln Arg Gln Ile Gln Ile
565 570 575
Leu Ala Glu Lys Leu Leu Ala Asp Asn Ile Val Pro Phe Phe Pro Glu
580 585 590
Thr Leu Thr Lys Tyr Gly Asp Leu Asp Leu Gln Arg Ile Met Glu Ile

```
        595                 600                 605
Lys Ser Glu Leu Ser Ser Ile Lys Thr Arg Arg Asn Asp Ser Tyr Asn
    610                 615                 620
Asn Tyr Ile Ala Arg Ala Ser Ile Val Thr Asp Leu Ser Lys Phe Asn
625                 630                 635                 640
Gln Ala Phe Arg Tyr Glu Thr Thr Ala Ile Cys Ala Asp Val Ala Asp
                645                 650                 655
Glu Leu His Gly Thr Gln Ser Leu Phe Cys Trp Leu His Leu Ile Val
            660                 665                 670
Pro Met Thr Thr Met Ile Cys Ala Tyr Arg His Ala Pro Pro Glu Thr
        675                 680                 685
Lys Gly Glu Tyr Asp Ile Asp Lys Ile Glu Glu Gln Ser Gly Leu Tyr
    690                 695                 700
Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu Trp Thr
705                 710                 715                 720
Met Glu Ala Ile Ser Leu Leu Asp Val Val Ser Val Lys Thr Arg Cys
                725                 730                 735
Gln Met Thr Ser Leu Leu Asn Gly Asp Asn Gln Ser Ile Asp Val Ser
            740                 745                 750
Lys Pro Val Lys Leu Ser Glu Gly Leu Asp Glu Val Lys Ala Asp Tyr
        755                 760                 765
Ser Leu Ala Val Lys Met Leu Lys Glu Ile Arg Asp Ala Tyr Arg Asn
    770                 775                 780
Ile Gly His Lys Leu Lys Glu Gly Glu Thr Tyr Ile Ser Arg Asp Leu
785                 790                 795                 800
Gln Phe Ile Ser Lys Val Ile Gln Ser Glu Gly Val Met His Pro Thr
                805                 810                 815
Pro Ile Lys Lys Ile Leu Arg Val Gly Pro Trp Ile Asn Thr Ile Leu
            820                 825                 830
Asp Asp Ile Lys Thr Ser Ala Glu Ser Ile Gly Ser Leu Cys Gln Glu
        835                 840                 845
Leu Glu Phe Arg Gly Glu Ser Ile Ile Val Ser Leu Ile Leu Arg Asn
    850                 855                 860
Phe Trp Leu Tyr Asn Leu Tyr Met His Glu Ser Lys Gln His Pro Leu
865                 870                 875                 880
Ala Gly Lys Gln Leu Phe Lys Gln Leu Asn Lys Thr Leu Thr Ser Val
                885                 890                 895
Gln Arg Phe Phe Glu Ile Lys Lys Glu Asn Glu Val Val Asp Leu Trp
            900                 905                 910
Met Asn Ile Pro Met Gln Phe Gly Gly Gly Asp Pro Val Val Phe Tyr
        915                 920                 925
Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala Ile Ser
    930                 935                 940
His Val Asp Ile Leu Leu Arg Ile Ser Ala Asn Ile Arg Asn Glu Ala
945                 950                 955                 960
Lys Ile Ser Phe Phe Lys Ala Leu Leu Ser Ile Glu Lys Asn Glu Arg
                965                 970                 975
Ala Thr Leu Thr Thr Leu Met Arg Asp Pro Gln Ala Val Gly Ser Glu
            980                 985                 990
Arg Gln Ala Lys Val Thr Ser Asp Ile Asn Arg Thr Ala Val Thr Ser
        995                 1000                1005
Ile Leu Ser Leu Ser Pro Asn Gln Leu Phe Ser Asp Ser Ala Ile His
    1010                1015                1020
Tyr Ser Arg Asn Glu Glu Glu Val Gly Ile Ile Ala Asp Asn Ile Thr
1025                1030                1035                1040
Pro Val Tyr Pro His Gly Leu Arg Val Leu Tyr Glu Ser Leu Pro Phe
                1045                1050                1055
His Lys Ala Glu Lys Val Val Asn Met Ile Ser Gly Thr Lys Ser Ile
            1060                1065                1070
Thr Asn Leu Leu Gln Arg Thr Ser Ala Ile Asn Gly Glu Asp Ile Asp
        1075                1080                1085
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Arg Ala Val Ser Met Met Leu Glu Asn Leu Gly Leu Leu Ser Arg Ile
1090 1095 1100
Leu Ser Val Val Val Asp Ser Ile Glu Ile Pro Thr Lys Ser Asn Gly
1105 1110 1115 1120
Arg Leu Ile Cys Cys Gln Ile Ser Arg Thr Leu Arg Glu Thr Ser Trp
1125 1130 1135
Asn Asn Met Glu Ile Val Gly Val Thr Ser Pro Ser Ile Thr Thr Cys
1140 1145 1150
Met Asp Val Ile Tyr Ala Thr Ser Ser His Leu Lys Gly Ile Ile Ile
1155 1160 1165
Glu Lys Phe Ser Thr Asp Arg Thr Thr Arg Gly Gln Arg Gly Pro Lys
1170 1175 1180
Ser Pro Trp Val Gly Ser Ser Thr Gln Glu Lys Lys Leu Val Pro Val
1185 1190 1195 1200
Tyr Asn Arg Gln Ile Leu Ser Lys Gln Gln Arg Glu Gln Leu Glu Ala
1205 1210 1215
Ile Gly Lys Met Arg Trp Val Tyr Lys Gly Thr Pro Gly Leu Arg Arg
1220 1225 1230
Leu Leu Asn Lys Ile Cys Leu Gly Ser Leu Gly Ile Ser Tyr Lys Cys
1235 1240 1245
Val Lys Pro Leu Leu Pro Arg Phe Met Ser Val Asn Phe Leu His Arg
1250 1255 1260
Leu Ser Val Ser Ser Arg Pro Met Glu Phe Pro Ala Ser Val Pro Ala
1265 1270 1275 1280
Tyr Arg Thr Thr Asn Tyr His Phe Asp Thr Ser Pro Ile Asn Gln Ala
1285 1290 1295
Leu Ser Glu Arg Phe Gly Asn Glu Asp Ile Asn Leu Val Phe Gln Asn
1300 1305 1310
Ala Ile Ser Cys Gly Ile Ser Ile Met Ser Val Val Glu Gln Leu Thr
1315 1320 1325
Gly Arg Ser Pro Lys Gln Leu Val Leu Ile Pro Gln Leu Glu Glu Ile
1330 1335 1340
Asp Ile Met Pro Pro Pro Val Phe Gln Gly Lys Phe Asn Tyr Lys Leu
1345 1350 1355 1360
Val Asp Lys Ile Thr Ser Asp Gln His Ile Phe Ser Pro Asp Lys Ile
1365 1370 1375
Asp Met Leu Thr Leu Gly Lys Met Leu Met Pro Thr Ile Lys Gly Gln
1380 1385 1390
Lys Thr Asp Gln Phe Leu Asn Lys Arg Glu Asn Tyr Phe His Gly Asn
1395 1400 1405
Asn Leu Ile Glu Ser Leu Ser Ala Ala Leu Ala Cys His Trp Cys Gly
1410 1415 1420
Ile Leu Thr Glu Gln Cys Ile Glu Asn Asn Ile Phe Lys Lys Asp Trp
1425 1430 1435 1440
Gly Asp Gly Phe Ile Ser Asp His Ala Phe Met Asp Phe Lys Ile Phe
1445 1450 1455
Leu Cys Val Phe Lys Thr Lys Leu Leu Cys Ser Trp Gly Ser Gln Gly
1460 1465 1470
Lys Asn Ile Lys Asp Glu Asp Ile Val Asp Glu Ser Ile Asp Lys Leu
1475 1480 1485
Leu Arg Ile Asp Asn Thr Phe Trp Arg Met Phe Ser Lys Val Met Phe
1490 1495 1500
Glu Ser Lys Val Lys Lys Arg Ile Met Leu Tyr Asp Val Lys Phe Leu
1505 1510 1515 1520
Ser Leu Val Gly Tyr Ile Gly Phe Lys Asn Trp Phe Ile Glu Gln Leu
1525 1530 1535
Arg Ser Ala Glu Leu His Glu Val Pro Trp Ile Val Asn Ala Glu Gly
1540 1545 1550
Asp Leu Val Glu Ile Lys Ser Ile Lys Ile Tyr Leu Gln Leu Ile Glu
1555 1560 1565
Gln Ser Leu Phe Leu Arg Ile Thr Val Leu Asn Tyr Thr Asp Met Ala

1570 1575 1580
His Ala Leu Thr Arg Leu Ile Arg Lys Lys Leu Met Cys Asp Asn Ala
1585 1590 1595 1600
Leu Leu Thr Pro Ile Pro Ser Pro Met Val Asn Leu Thr Gln Val Ile
1605 1610 1615
Asp Pro Thr Glu Gln Leu Ala Tyr Phe Pro Lys Ile Thr Phe Glu Arg
1620 1625 1630
Leu Lys Asn Tyr Asp Thr Ser Ser Asn Tyr Ala Lys Gly Lys Leu Thr
1635 1640 1645
Arg Asn Tyr Met Ile Leu Leu Pro Trp Gln His Val Asn Arg Tyr Asn
1650 1655 1660
Phe Val Phe Ser Ser Thr Gly Cys Lys Val Ser Leu Lys Thr Cys Ile
1665 1670 1675 1680
Gly Lys Leu Met Lys Asp Leu Asn Pro Lys Val Leu Tyr Phe Ile Gly
1685 1690 1695
Glu Gly Ala Gly Asn Trp Met Ala Arg Thr Ala Cys Glu Tyr Pro Asp
1700 1705 1710
Ile Lys Phe Val Tyr Arg Ser Leu Lys Asp Asp Leu Asp His His Tyr
1715 1720 1725
Pro Leu Glu Tyr Gln Arg Val Ile Gly Glu Leu Ser Arg Ile Ile Asp
1730 1735 1740
Ser Gly Glu Gly Leu Ser Met Glu Thr Thr Asp Ala Thr Gln Lys Thr
1745 1750 1755 1760
His Trp Asp Leu Ile His Arg Val Ser Lys Asp Ala Leu Leu Ile Thr
1765 1770 1775
Leu Cys Asp Ala Glu Phe Lys Asp Arg Asp Asp Phe Phe Lys Met Val
1780 1785 1790
Ile Leu Trp Arg Lys His Val Leu Ser Cys Arg Ile Cys Thr Thr Tyr
1795 1800 1805
Gly Thr Asp Leu Tyr Leu Phe Ala Lys Tyr His Ala Lys Asp Cys Asn
1810 1815 1820
Val Lys Leu Pro Phe Phe Val Arg Ser Val Ala Thr Phe Ile Met Gln
1825 1830 1835 1840
Gly Ser Lys Leu Ser Gly Ser Glu Cys Tyr Ile Leu Leu Thr Leu Gly
1845 1850 1855
His His Asn Asn Leu Pro Cys His Gly Glu Ile Gln Asn Ser Lys Met
1860 1865 1870
Lys Ile Ala Val Cys Asn Asp Phe Tyr Ala Ala Lys Lys Leu Asp Asn
1875 1880 1885
Lys Ser Ile Glu Ala Asn Cys Lys Ser Leu Leu Ser Gly Leu Arg Ile
1890 1895 1900
Pro Ile Asn Lys Lys Glu Leu Asn Arg Gln Arg Arg Leu Leu Thr Leu
1905 1910 1915 1920
Gln Ser Asn His Ser Ser Val Ala Thr Val Gly Gly Ser Lys Val Ile
1925 1930 1935
Glu Ser Lys Trp Leu Thr Asn Lys Ala Asn Thr Ile Ile Asp Trp Leu
1940 1945 1950
Glu His Ile Leu Asn Ser Pro Lys Gly Glu Leu Asn Tyr Asp Phe Phe
1955 1960 1965
Glu Ala Leu Glu Asn Thr Tyr Pro Asn Met Ile Lys Leu Ile Asp Asn
1970 1975 1980
Leu Gly Asn Ala Glu Ile Lys Lys Leu Ile Lys Val Thr Gly Tyr Met
1985 1990 1995 2000
Leu Val Ser Lys Lys
2005

<210> 406
<211> 13350
<212> DNA
<213> Human metapneumovirus

<220>
<223> RNA-dependent RNA polymerase (L) of Human metapneumovirus

<400> 406
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ctgagtgatt tatcatacaa gcatgctata ttaaaagagt ctcagtacac aataaaaaga 120
gatgtgggta caacaactgc agtgacaccc tcatcattgc aacaagaaat aacactgttg 180
tgtggagaaa ttctgtatgc taaacatgct gactacaaat atgctgcaga aataggaata 240
caatatatta gcacagcttt aggatcagag agagtgcagc agattctgag gaactcaggc 300
agtgaagtcc aagtggtctt aaccagaacg tactctctgg ggaaaattaa aaacaataaa 360
ggagaagatt tacagatgtt agacatacac ggggtagaga agagctgggt agaagagata 420
gacaaagaag caaggaaaac aatggcaacc ttgcttaagg aatcatcagg taatatccca 480
caaaatcaga ggccctcagc accagacaca cccataatct tattatgtgt aggtgcctta 540
atattcacta aactagcatc aaccatagaa gtgggactag agaccacagt cagaagggct 600
aaccgtgtac taagtgatgc actcaagaga taccctagaa tggacatacc aaagattgcc 660
agatccttct atgacttatt tgaacaaaaa gtgtatcaca gaagtttgtt cattgagtat 720
ggcaaagcat taggctcatc atctacaggc agcaaagcag aaagtctatt tgttaatata 780
ttcatgcaag cttatggggc cggtcaaaca atgctaaggt ggggggtcat tgccaggtca 840
tccaacaata taatgttagg acatgtatcc gtccaagctg agttaaaaca ggtcacagaa 900
gtctatgact tggtgcgaga aatgggccct gaatctggac ttctacattt aaggcaaagc 960
ccaaaagctg gactgttatc actagccaac tgtcccaact ttgcaagtgt tgttctcgga 1020
aatgcctcag gcttaggcat aatcggtatg tatcgaggga gagtaccaaa cacagaatta 1080
ttttcagcag ctgaaagtta tgccaaaagt ttgaaagaaa gcaataaaat aaatttctct 1140
tcattaggac ttacagatga agagaaagag gctgcagaac atttcttaaa tgtgagtgac 1200
gacagtcaaa atgattatga gtaattaaaa aagtgggaca agtcaaaatg tcattccctg 1260
aaggaaaaga tattcttttc atgggtaatg aagcagcaaa attagcagaa gctttccaga 1320
aatcattaag aaaaccaggt cataaaagat ctcaatctat tataggagaa aaagtgaata 1380
ctgtatcaga aacattggaa ttacctacta tcagtagacc tgcaaaacca accataccgt 1440
cagaaccaaa gttagcatgg acagataaag gtggggcaac caaaactgaa ataaagcaag 1500
caatcaaagt catggatccc attgaagaag aagagtctac cgagaagaag gtgctaccct 1560
ccagtgatgg gaaaacccct gcagaaaaga aactgaaacc atcaactaac accaaaaaga 1620
aggtttcatt tacaccaaat gaaccaggga aatatacaaa gttggaaaaa gatgctctag 1680
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115 120 125
Gln Glu Leu Trp Leu Asn Ile Leu Arg Gln Leu Gly Cys Val Glu Gly
130 135 140
Lys Glu Gly Phe Asp Ser Leu Lys Asp Val Asp Ile Ile Pro Asp Ile
145 150 155 160
Thr Asp Lys Tyr Asn Lys Asn Thr Trp Tyr Arg Pro Phe Leu Thr Trp
165 170 175
Phe Ser Ile Lys Tyr Asp Met Arg Trp Met Gln Lys Asn Lys Ser Gly
180 185 190
Asn His Leu Asp Val Ser Asn Ser His Asn Phe Leu Asp Cys Lys Ser
195 200 205
Tyr Ile Leu Ile Ile Tyr Arg Asp Leu Val Ile Ile Ile Asn Lys Leu
210 215 220
Lys Leu Thr Gly Tyr Val Leu Thr Pro Glu Leu Val Leu Met Tyr Cys
225 230 235 240
Asp Val Val Glu Gly Arg Trp Asn Met Ser Ser Ala Gly Arg Leu Asp
245 250 255
Lys Arg Ser Ser Lys Ile Thr Cys Lys Gly Glu Glu Leu Trp Glu Leu
260 265 270
Ile Asp Ser Leu Phe Pro Asn Leu Gly Glu Asp Val Tyr Asn Ile Ile
275 280 285
Ser Leu Leu Glu Pro Leu Ser Leu Ala Leu Ile Gln Leu Asp Asp Pro
290 295 300
Val Thr Asn Leu Lys Gly Ala Phe Met Arg His Val Leu Thr Glu Leu
305 310 315 320
His Thr Ile Leu Ile Lys Asp Asn Ile Tyr Thr Asp Ser Glu Ala Asp
325 330 335
Ser Ile Met Glu Ser Leu Ile Lys Ile Phe Arg Glu Thr Ser Ile Asp
340 345 350
Glu Lys Ala Glu Ile Phe Ser Phe Phe Arg Thr Phe Gly His Pro Ser
355 360 365

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Leu Glu Ala Ile Thr Ala Ala Asp Lys Val Arg Thr His Met Tyr Ser
    370                 375                 380
Ser Lys Lys Ile Ile Leu Lys Thr Leu Tyr Glu Cys His Ala Ile Phe
385                 390                 395                 400
Cys Ala Ile Ile Ile Asn Gly Tyr Arg Glu Arg His Gly Gly Gln Trp
                405                 410                 415
Pro Pro Cys Glu Phe Pro Asn His Val Cys Leu Glu Leu Lys Asn Ala
            420                 425                 430
Gln Gly Ser Asn Ser Ala Ile Ser Tyr Glu Cys Ala Val Asp Asn Tyr
        435                 440                 445
Ser Ser Phe Ile Gly Phe Lys Phe Leu Lys Phe Ile Glu Pro Gln Leu
    450                 455                 460
Asp Glu Asp Leu Thr Ile Tyr Met Lys Asp Lys Ala Leu Ser Pro Arg
465                 470                 475                 480
Lys Ala Ala Trp Asp Ser Val Tyr Pro Asp Ser Asn Leu Tyr Tyr Lys
                485                 490                 495
Val Pro Glu Ser Glu Glu Thr Arg Arg Leu Ile Glu Val Phe Ile Asn
            500                 505                 510
Asp Asn Asn Phe Asn Pro Ala Asp Ile Ile Asn Tyr Val Glu Ser Gly
        515                 520                 525
Glu Trp Leu Asn Asp Asp Ser Phe Asn Ile Ser Tyr Ser Leu Lys Glu
    530                 535                 540
Lys Glu Ile Lys Gln Glu Gly Arg Leu Phe Ala Lys Met Thr Tyr Lys
545                 550                 555                 560
Met Arg Ala Val Gln Val Leu Ala Glu Thr Leu Leu Ala Lys Gly Val
                565                 570                 575
Gly Glu Leu Phe Ser Glu Asn Gly Met Val Lys Gly Glu Ile Asp Leu
            580                 585                 590
Leu Lys Arg Leu Thr Thr Leu Ser Val Ser Gly Val Pro Arg Ser Asn
        595                 600                 605
Ser Val Tyr Asn Asn Pro Ile Leu His Glu Lys Leu Ile Lys Asn Met
    610                 615                 620
Asn Lys Cys Asn Ser Asn Gly Tyr Trp Asp Glu Arg Lys Lys Ser Lys
625                 630                 635                 640
Asn Glu Phe Lys Ala Ala Asp Ser Ser Thr Glu Gly Tyr Glu Thr Leu
                645                 650                 655
Ser Cys Phe Leu Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
            660                 665                 670
Phe Glu Ser Thr Ala Leu Phe Gly Gln Arg Cys Asn Glu Ile Phe Gly
        675                 680                 685
Phe Lys Thr Phe Phe Asn Trp Met His Pro Ile Leu Glu Lys Ser Thr
    690                 695                 700
Ile Tyr Val Gly Asp Pro Tyr Cys Pro Val Pro Asp Arg Met His Lys
705                 710                 715                 720
Glu Leu Gln Asp His Asp Asp Thr Gly Ile Phe Ile His Asn Pro Arg
                725                 730                 735
Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Leu Ile Ser Ile
            740                 745                 750
Ser Ala Ile His Leu Ala Ala Val Lys Val Gly Val Arg Val Ser Ala
        755                 760                 765
Met Val Gln Gly Asp Asn Gln Ala Ile Ala Val Thr Ser Arg Val Pro
    770                 775                 780
Val Thr Gln Thr Tyr Lys Gln Lys Lys Thr His Val Tyr Glu Glu Ile
785                 790                 795                 800
Thr Arg Tyr Phe Gly Ala Leu Arg Glu Val Met Phe Asp Ile Gly His
                805                 810                 815
Glu Leu Lys Leu Asn Glu Thr Ile Ile Ser Ser Lys Met Phe Val Tyr
            820                 825                 830
Ser Lys Arg Ile Tyr Tyr Asp Gly Lys Ile Leu Pro Gln Cys Leu Lys
        835                 840                 845
Ala Leu Thr Arg Cys Val Phe Trp Ser Glu Thr Leu Val Asp Glu Asn
```

850 855 860
Arg Ser Ala Cys Ser Asn Ile Ala Thr Ser Ile Ala Lys Ala Ile Glu
865 870 875 880
Asn Gly Tyr Ser Pro Ile Leu Gly Tyr Cys Ile Ala Leu Phe Lys Thr
885 890 895
Cys Gln Gln Val Cys Ile Ser Leu Gly Met Thr Ile Asn Pro Thr Ile
900 905 910
Thr Ser Thr Ile Lys Asp Gln Tyr Phe Lys Gly Lys Asn Trp Leu Arg
915 920 925
Cys Ala Ile Leu Ile Pro Ala Asn Ile Gly Gly Phe Asn Tyr Met Ser
930 935 940
Thr Ala Arg Cys Phe Val Arg Asn Ile Gly Asp Pro Ala Val Ala Ala
945 950 955 960
Leu Ala Asp Leu Lys Arg Phe Ile Lys Ala Gly Leu Leu Asp Lys Gln
965 970 975
Val Leu Tyr Arg Val Met Asn Gln Glu Pro Gly Asp Ser Ser Phe Leu
980 985 990
Asp Trp Ala Ser Asp Pro Tyr Ser Cys Asn Leu Pro His Ser Gln Ser
995 1000 1005
Ile Thr Thr Ile Ile Lys Asn Val Thr Ala Arg Ser Val Leu Gln Glu
1010 1015 1020
Ser Pro Asn Pro Leu Leu Ser Gly Leu Phe Ser Glu Ser Ser Ser Glu
1025 1030 1035 1040
Glu Asp Leu Asn Leu Ala Ser Phe Leu Met Asp Arg Lys Ala Ile Leu
1045 1050 1055
Pro Arg Val Ala His Glu Ile Leu Asp Asn Ser Leu Thr Gly Val Arg
1060 1065 1070
Glu Ala Ile Ala Gly Met Leu Asp Thr Thr Lys Ser Leu Val Arg Ala
1075 1080 1085
Ser Val Arg Arg Gly Gly Leu Ser Tyr Ser Ile Leu Arg Arg Leu Ile
1090 1095 1100
Asn Tyr Asp Leu Leu Gln Tyr Glu Thr Leu Thr Arg Thr Leu Arg Lys
1105 1110 1115 1120
Pro Val Lys Asp Asn Ile Glu Tyr Glu Tyr Met Cys Ser Val Glu Leu
1125 1130 1135
Ala Ile Gly Leu Arg Gln Lys Met Trp Phe His Leu Thr Tyr Gly Arg
1140 1145 1150
Pro Ile His Gly Leu Glu Thr Pro Asp Pro Leu Glu Leu Leu Arg Gly
1155 1160 1165
Ser Phe Ile Glu Gly Ser Glu Ile Cys Lys Phe Cys Arg Ser Glu Gly
1170 1175 1180
Asn Asn Pro Met Tyr Thr Trp Phe Tyr Leu Pro Asp Asn Ile Asp Leu
1185 1190 1195 1200
Asp Thr Leu Ser Asn Gly Ser Pro Ala Ile Arg Ile Pro Tyr Phe Gly
1205 1210 1215
Ser Ala Thr Asp Glu Arg Ser Glu Ala Gln Leu Gly Tyr Val Lys Asn
1220 1225 1230
Leu Ser Lys Pro Ala Lys Ala Ala Ile Arg Ile Ala Met Val Tyr Thr
1235 1240 1245
Trp Ala Tyr Gly Thr Asp Glu Ile Ser Trp Met Glu Ala Ala Leu Ile
1250 1255 1260
Ala Gln Thr Arg Ala Asn Leu Ser Leu Glu Asn Leu Lys Leu Leu Thr
1265 1270 1275 1280
Pro Val Ser Thr Ser Thr Asn Leu Ser His Arg Leu Arg Asp Thr Ala
1285 1290 1295
Thr Gln Met Lys Phe Ser Ser Ala Thr Leu Val Arg Ala Ser Arg Phe
1300 1305 1310
Ile Thr Ile Ser Asn Asp Asn Met Ala Leu Lys Glu Ala Gly Glu Ser
1315 1320 1325
Lys Asp Thr Asn Leu Val Tyr Gln Gln Ile Met Leu Thr Gly Leu Ser
1330 1335 1340

Leu Phe Glu Phe Asn Met Arg Tyr Lys Gln Gly Ser Leu Ser Lys Pro
1345 1350 1355 1360
Met Ile Leu His Leu His Leu Asn Asn Lys Cys Cys Ile Ile Glu Ser
1365 1370 1375
Pro Gln Glu Leu Asn Ile Pro Pro Arg Ser Thr Leu Asp Leu Glu Ile
1380 1385 1390
Thr Gln Glu Asn Asn Lys Leu Ile Tyr Asp Pro Asp Pro Leu Lys Asp
1395 1400 1405
Ile Asp Leu Glu Leu Phe Ser Lys Val Arg Asp Val Val His Thr Ile
1410 1415 1420
Asp Met Asn Tyr Trp Ser Asp Asp Glu Ile Ile Arg Ala Thr Ser Ile
1425 1430 1435 1440
Cys Thr Ala Met Thr Ile Ala Asp Thr Met Ser Gln Leu Asp Arg Asp
1445 1450 1455
Asn Leu Lys Glu Met Ile Ala Leu Ile Asn Asp Asp Asp Ile Asn Ser
1460 1465 1470
Leu Ile Thr Glu Phe Met Val Ile Asp Ile Pro Leu Phe Cys Ser Thr
1475 1480 1485
Phe Gly Gly Ile Leu Ile Asn Gln Phe Ala Tyr Ser Leu Tyr Gly Leu
1490 1495 1500
Asn Val Arg Gly Arg Asp Glu Ile Trp Gly Tyr Val Ile Arg Ile Ile
1505 1510 1515 1520
Lys Asp Thr Ser His Ala Val Leu Lys Val Leu Ser Asn Ala Leu Ser
1525 1530 1535
His Pro Lys Ile Phe Lys Arg Phe Trp Asp Ala Gly Val Val Glu Pro
1540 1545 1550
Val Tyr Gly Pro Asn Leu Ser Asn Gln Asp Lys Ile Leu Leu Ala Ile
1555 1560 1565
Ser Val Cys Glu Tyr Ser Val Asp Leu Phe Met Arg Asp Trp Gln Glu
1570 1575 1580
Gly Ile Pro Leu Glu Ile Phe Ile Cys Asp Asn Asp Pro Asn Ile Ala
1585 1590 1595 1600
Glu Met Arg Lys Leu Ser Phe Leu Ala Arg His Leu Ala Tyr Leu Cys
1605 1610 1615
Ser Leu Ala Glu Ile Ala Lys Glu Gly Pro Lys Leu Glu Ser Met Thr
1620 1625 1630
Ser Leu Glu Arg Leu Glu Ser Leu Lys Glu Tyr Leu Glu Leu Thr Phe
1635 1640 1645
Leu Asp Asp Pro Ile Leu Arg Tyr Ser Gln Leu Thr Gly Leu Val Ile
1650 1655 1660
Lys Ile Phe Pro Ser Thr Leu Thr Tyr Ile Arg Lys Ser Ser Ile Lys
1665 1670 1675 1680
Val Leu Arg Val Arg Gly Ile Gly Ile Pro Glu Val Leu Glu Asp Trp
1685 1690 1695
Asp Pro Asp Ala Asp Ser Met Leu Leu Asp Asn Ile Thr Ala Glu Val
1700 1705 1710
Gln His Asn Ile Pro Leu Lys Lys Asn Glu Arg Thr Pro Phe Trp Gly
1715 1720 1725
Leu Arg Val Ser Lys Ser Gln Val Leu Arg Leu Arg Gly Tyr Glu Glu
1730 1735 1740
Ile Lys Arg Glu Glu Arg Gly Arg Ser Gly Val Gly Leu Thr Leu Pro
1745 1750 1755 1760
Phe Asp Gly Arg Tyr Leu Ser His Gln Leu Arg Leu Phe Gly Ile Asn
1765 1770 1775
Ser Thr Ser Cys Leu Lys Ala Leu Glu Leu Thr Tyr Leu Leu Asn Pro
1780 1785 1790
Leu Val Asn Lys Asp Lys Asp Arg Leu Tyr Leu Gly Glu Gly Ala Gly
1795 1800 1805
Ala Met Leu Ser Cys Tyr Asp Ala Thr Leu Gly Pro Cys Met Asn Tyr
1810 1815 1820
Tyr Asn Ser Gly Val Asn Ser Cys Asp Leu Asn Gly Gln Arg Glu Leu

1825 1830 1835 1840
Asn Ile Tyr Pro Ser Glu Val Ala Leu Val Gly Lys Lys Leu Asn Asn
1845 1850 1855
Val Thr Ser Leu Cys Gln Arg Val Lys Val Leu Phe Asn Gly Asn Pro
1860 1865 1870
Gly Ser Thr Trp Ile Gly Asn Asp Glu Cys Glu Thr Leu Ile Trp Asn
1875 1880 1885
Glu Leu Gln Asn Asn Ser Ile Gly Phe Ile His Cys Asp Met Glu Gly
1890 1895 1900
Gly Glu His Lys Cys Asp Gln Val Val Leu His Glu His Tyr Ser Val
1905 1910 1915 1920
Ile Arg Ile Ala Tyr Leu Val Gly Asp Lys Asp Val Ile Leu Val Ser
1925 1930 1935
Lys Ile Ala Pro Arg Leu Gly Thr Asp Trp Thr Lys Gln Leu Ser Leu
1940 1945 1950
Tyr Leu Arg Tyr Trp Arg Asp Val Ser Leu Ile Val Leu Lys Thr Ser
1955 1960 1965
Asn Pro Ala Ser Thr Glu Met Tyr Leu Ile Ser Lys Asp Pro Lys Ser
1970 1975 1980
Asp Ile Ile Glu Asp Ser Asn Thr Val Leu Ala Asn Leu Leu Pro Leu
1985 1990 1995 2000
Ser Lys Glu Asp Ser Ile Lys Ile Glu Lys Trp Ile Leu Val Glu Lys
2005 2010 2015
Ala Lys Val His Asp Trp Ile Val Arg Glu Leu Lys Glu Gly Ser Ala
2020 2025 2030
Ser Ser Gly Met Leu Arg Pro Tyr His Gln Ala Leu Gln Ile Phe Gly
2035 2040 2045
Phe Glu Pro Asn Leu Asn Lys Leu Cys Arg Asp Phe Leu Ser Thr Leu
2050 2055 2060
Asn Ile Val Asp Thr Lys Asn Cys Ile Ile Thr Phe Asp Arg Val Leu
2065 2070 2075 2080
Arg Asp Thr Ile Phe Glu Trp Thr Arg Ile Lys Asp Ala Asp Lys Lys
2085 2090 2095
Leu Arg Leu Thr Gly Lys Tyr Asp Leu Tyr Pro Leu Arg Asp Ser Gly
2100 2105 2110
Lys Leu Lys Val Ile Ser Arg Arg Leu Val Ile Ser Trp Ile Ala Leu
2115 2120 2125
Ser Met Ser Thr Arg Leu Val Thr Gly Ser Phe Pro Asp Ile Lys Phe
2130 2135 2140
Glu Ser Arg Leu Gln Leu Gly Ile Val Ser Ile Ser Ser Arg Glu Ile
2145 2150 2155 2160
Lys Asn Leu Arg Val Ile Ser Lys Ile Val Ile Asp Lys Phe Glu Asp
2165 2170 2175
Ile Ile His Ser Val Thr Tyr Arg Phe Leu Thr Lys Glu Ile Lys Ile
2180 2185 2190
Leu Met Lys Ile Leu Gly Ala Val Lys Leu Phe Gly Ala Arg Gln Ser
2195 2200 2205
Thr Ser Ala Asp Ile Thr Asn Ile Asp Thr Ser Asp Ser Ile Gln
2210 2215 2220

<210> 409
<211> 575
<212> PRT
<213> Human parainfluenza virus 1 strain Washington/1964

<220>
<223> HN glycoprotein of Human parainfluenza 1 virus

<400> 409
Met Ala Glu Lys Gly Lys Thr Asn Ser Ser Tyr Trp Ser Thr Thr Arg

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1               5                   10                  15
Asn Asp Asn Ser Thr Val Asn Thr His Ile Asn Thr Pro Ala Gly Arg
            20                  25                  30
Thr His Ile Trp Leu Leu Ile Ala Thr Thr Met His Thr Val Leu Ser
        35                  40                  45
Phe Ile Ile Met Ile Leu Cys Ile Asp Leu Ile Ile Lys Gln Asp Thr
    50                  55                  60
Cys Met Lys Thr Asn Ile Met Thr Val Ser Ser Met Asn Glu Ser Ala
65                  70                  75                  80
Lys Ile Ile Lys Glu Thr Ile Thr Glu Leu Ile Arg Gln Glu Val Ile
                85                  90                  95
Ser Arg Thr Ile Asn Ile Gln Ser Ser Val Gln Ser Gly Ile Pro Ile
            100                 105                 110
Leu Leu Asn Lys Gln Ser Arg Asp Leu Thr Gln Leu Ile Glu Lys Ser
        115                 120                 125
Cys Asn Arg Gln Glu Leu Ala Gln Ile Cys Glu Asn Thr Ile Ala Ile
    130                 135                 140
His His Ala Asp Gly Ile Ser Pro Leu Asp Pro His Asp Phe Trp Arg
145                 150                 155                 160
Cys Pro Val Gly Glu Pro Leu Leu Ser Asn Asn Pro Asn Ile Ser Leu
                165                 170                 175
Leu Pro Gly Pro Ser Leu Leu Ser Gly Ser Thr Thr Ile Ser Gly Cys
            180                 185                 190
Val Arg Leu Pro Ser Leu Ser Ile Gly Asp Ala Ile Tyr Ala Tyr Ser
        195                 200                 205
Ser Asn Leu Ile Thr Gln Gly Cys Ala Asp Ile Gly Lys Ser Tyr Gln
    210                 215                 220
Val Leu Gln Leu Gly Tyr Ile Ser Leu Asn Ser Asp Met Tyr Pro Asp
225                 230                 235                 240
Leu Asn Pro Val Ile Ser His Thr Tyr Asp Ile Asn Asp Asn Arg Lys
                245                 250                 255
Ser Cys Ser Val Ile Ala Ala Gly Thr Arg Gly Tyr Gln Leu Cys Ser
            260                 265                 270
Leu Pro Thr Val Asn Glu Thr Thr Asp Tyr Ser Ser Glu Gly Ile Glu
        275                 280                 285
Asp Leu Val Phe Asp Ile Leu Asp Leu Lys Gly Lys Thr Lys Ser His
    290                 295                 300
Arg Tyr Lys Asn Glu Asp Ile Thr Phe Asp His Pro Phe Ser Ala Met
305                 310                 315                 320
Tyr Pro Ser Val Gly Ser Gly Ile Lys Ile Glu Asn Thr Leu Ile Phe
                325                 330                 335
Leu Gly Tyr Gly Gly Leu Thr Thr Pro Leu Gln Gly Asp Thr Lys Cys
            340                 345                 350
Val Ile Asn Arg Cys Thr Asn Val Asn Gln Ser Val Cys Asn Asp Ala
        355                 360                 365
Leu Lys Ile Thr Trp Leu Lys Lys Arg Gln Val Val Asn Val Leu Ile
    370                 375                 380
Arg Ile Asn Asn Tyr Leu Ser Asp Arg Pro Lys Ile Val Val Glu Thr
385                 390                 395                 400
Ile Pro Ile Thr Gln Asn Tyr Leu Gly Ala Glu Gly Arg Leu Leu Lys
                405                 410                 415
Leu Gly Lys Lys Ile Tyr Ile Tyr Thr Arg Ser Ser Gly Trp His Ser
            420                 425                 430
Asn Leu Gln Ile Gly Ser Leu Asp Ile Asn Asn Pro Met Thr Ile Lys
        435                 440                 445
Trp Ala Pro His Glu Val Leu Ser Arg Pro Gly Asn Gln Asp Cys Asn
    450                 455                 460
Trp Tyr Asn Arg Cys Pro Arg Glu Cys Ile Ser Gly Val Tyr Thr Asp
465                 470                 475                 480
Ala Tyr Pro Leu Ser Pro Asp Ala Val Asn Val Ala Thr Thr Thr Leu
                485                 490                 495
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Tyr Ala Asn Thr Ser Arg Val Asn Pro Thr Ile Met Tyr Ser Asn Thr
500 505 510
Ser Glu Ile Ile Asn Met Leu Arg Leu Lys Asn Val Gln Leu Glu Ala
515 520 525
Ala Tyr Thr Thr Thr Ser Cys Ile Thr His Phe Gly Lys Gly Tyr Cys
530 535 540
Phe His Ile Val Glu Ile Asn Gln Ala Ser Leu Asn Thr Leu Gln Pro
545 550 555 560
Met Leu Phe Lys Thr Ser Ile Pro Lys Ile Cys Lys Ile Thr Ser
565 570 575

<210> 410
<211> 348
<212> PRT
<213> Human parainfluenza virus 1 strain Washington/1964

<220>
<223> matrix protein of Human parainfluenza 1 virus

<400> 410
Met Ala Glu Thr Tyr Arg Phe Pro Arg Phe Ser His Glu Glu Asn Gly
1 5 10 15
Thr Val Glu Pro Leu Pro Leu Lys Thr Gly Pro Asp Lys Lys Ala Ile
20 25 30
Pro His Ile Arg Ile Val Lys Val Gly Asp Pro Pro Lys His Gly Val
35 40 45
Arg Tyr Leu Asp Val Leu Leu Leu Gly Phe Phe Glu Thr Pro Lys Gln
50 55 60
Gly Pro Leu Ser Gly Ser Ile Ser Asp Leu Thr Glu Ser Thr Ser Tyr
65 70 75 80
Ser Ile Cys Gly Ser Gly Ser Leu Pro Ile Gly Ile Ala Lys Tyr Tyr
85 90 95
Gly Thr Asp Gln Glu Leu Leu Lys Ala Cys Ile Asp Leu Lys Ile Thr
100 105 110
Val Arg Arg Thr Val Arg Ser Gly Glu Met Ile Val Tyr Met Val Asp
115 120 125
Ser Ile His Ala Pro Leu Leu Pro Trp Ser Ser Arg Leu Arg Gln Gly
130 135 140
Met Ile Tyr Asn Ala Asn Lys Val Ala Leu Ala Pro Gln Cys Leu Pro
145 150 155 160
Val Asp Lys Asp Ile Arg Phe Arg Val Val Phe Val Asn Gly Thr Ser
165 170 175
Leu Gly Thr Ile Thr Ile Ala Lys Val Pro Lys Thr Leu Ala Asp Leu
180 185 190
Ala Leu Pro Asn Ser Ile Ser Val Asn Leu Leu Val Thr Leu Arg Ala
195 200 205
Gly Val Ser Thr Glu Gln Lys Gly Ile Leu Pro Val Leu Asp Asp Asp
210 215 220
Gly Glu Lys Lys Leu Asn Phe Met Val His Leu Gly Ile Ile Arg Arg
225 230 235 240
Lys Val Gly Lys Ile Tyr Ser Val Glu Tyr Cys Lys Asn Lys Ile Glu
245 250 255
Lys Met Lys Leu Ile Phe Ser Leu Gly Leu Val Gly Gly Ile Ser Phe
260 265 270
His Val His Ala Thr Gly Thr Leu Ser Lys Thr Leu Met Ser Gln Leu
275 280 285
Ala Trp Lys Lys Ala Val Cys Tyr Pro Leu Met Asp Val Asn Pro His
290 295 300
Met Asn Leu Val Ile Trp Ala Ala Ser Val Glu Ile Thr Ser Val Asp
305 310 315 320

Ala Val Phe Gln Pro Ala Ile Pro Lys Glu Phe Arg Tyr Tyr Pro Asn
325 330 335
Val Val Ala Lys Ser Ile Gly Lys Ile Arg Arg Ile
340 345

<210> 411
<211> 181
<212> PRT
<213> Human parainfluenza virus 1 strain Washington/1964

<220>
<223> Y1 protein of Human parainfluenza 1 virus

<400> 411
Met Ser Ser Asp Ser Leu Thr Ser Ser Tyr Pro Thr Ser Pro Gln Lys
1 5 10 15
Leu Glu Lys Thr Glu Ala Gly Ser Met Val Ser Ser Thr Thr Gln Lys
20 25 30
Lys Thr Ser His His Ala Lys Pro Thr Ile Thr Thr Lys Thr Glu Gln
35 40 45
Ser Gln Arg Arg Pro Lys Ile Ile Asp Gln Val Arg Gly Val Glu Ser
50 55 60
Leu Gly Glu Gln Val Ser Gln Lys Gln Arg His Met Leu Glu Ser Leu
65 70 75 80
Ile Asn Lys Val Tyr Thr Gly Pro Leu Gly Glu Glu Leu Val Gln Thr
85 90 95
Leu Tyr Leu Arg Ile Trp Ala Met Lys Glu Thr Pro Glu Ser Thr Lys
100 105 110
Ile Leu Gln Met Arg Glu Asp Ile Arg Asp Gln Tyr Leu Arg Met Lys
115 120 125
Thr Glu Arg Trp Leu Arg Thr Leu Ile Arg Gly Lys Lys Thr Lys Leu
130 135 140
Arg Asp Phe Gln Lys Arg Tyr Glu Glu Val His Pro Tyr Leu Met Met
145 150 155 160
Glu Arg Val Glu Gln Ile Ile Met Glu Glu Ala Trp Lys Leu Ala Ala
165 170 175
His Ile Val Gln Glu
180

<210> 412
<211> 204
<212> PRT
<213> Human parainfluenza virus 1 strain Washington/1964

<220>
<223> C protein of Human parainfluenza 1 virus

<400> 412
Met Pro Ser Phe Leu Arg Gly Ile Leu Lys Pro Lys Glu Arg His His
1 5 10 15
Glu Asn Lys Asn His Ser Gln Met Ser Ser Asp Ser Leu Thr Ser Ser
20 25 30
Tyr Pro Thr Ser Pro Gln Lys Leu Glu Lys Thr Glu Ala Gly Ser Met
35 40 45
Val Ser Ser Thr Thr Gln Lys Lys Thr Ser His His Ala Lys Pro Thr
50 55 60
Ile Thr Thr Lys Thr Glu Gln Ser Gln Arg Arg Pro Lys Ile Ile Asp
65 70 75 80
Gln Val Arg Gly Val Glu Ser Leu Gly Glu Gln Val Ser Gln Lys Gln
85 90 95
Arg His Met Leu Glu Ser Leu Ile Asn Lys Val Tyr Thr Gly Pro Leu

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            100                     105                     110
Gly Glu Glu Leu Val Gln Thr Leu Tyr Leu Arg Ile Trp Ala Met Lys
        115                     120                     125
Glu Thr Pro Glu Ser Thr Lys Ile Leu Gln Met Arg Glu Asp Ile Arg
    130                     135                     140
Asp Gln Tyr Leu Arg Met Lys Thr Glu Arg Trp Leu Arg Thr Leu Ile
145                     150                     155                     160
Arg Gly Lys Lys Thr Lys Leu Arg Asp Phe Gln Lys Arg Tyr Glu Glu
                165                     170                     175
Val His Pro Tyr Leu Met Met Glu Arg Val Glu Gln Ile Ile Met Glu
            180                     185                     190
Glu Ala Trp Lys Leu Ala Ala His Ile Val Gln Glu
        195                     200
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<210> 413
<211> 568
<212> PRT
<213> Human parainfluenza virus 1 strain Washington/1964

<220>
<223>  phosphoprotein of Human parainfluenza 1 virus

<400> 413
Met Asp Gln Asp Ala Phe Phe Phe Glu Arg Asp Pro Glu Ala Glu Gly
 1               5                  10                  15
Glu Ala Pro Arg Lys Gln Glu Ser Leu Ser Asp Val Ile Gly Leu Leu
            20                  25                  30
Asp Val Val Leu Ser Tyr Lys Pro Thr Glu Ile Gly Glu Asp Arg Ser
        35                  40                  45
Trp Leu His Gly Ile Ile Asp Asn Pro Lys Glu Asn Lys Pro Ser Cys
    50                  55                  60
Lys Ala Asp Asp Asn Asn Lys Asp Arg Ala Ile Ser Thr Ser Thr Gln
65                  70                  75                  80
Asp His Arg Ser Ser Glu Gly Ser Gly Ile Ser Arg Arg Thr Ser Glu
                85                  90                  95
Ser Lys Thr Glu Thr His Ala Arg Ile Leu Asp Gln Gln Gly Ile His
            100                 105                 110
Arg Ala Ser Arg Arg Gly Thr Ser Pro Asn Pro Leu Pro Glu Asn Met
        115                 120                 125
Gly Asn Glu Arg Asn Thr Arg Ile Asp Glu Asp Ser Pro Asn Glu Arg
    130                 135                 140
Arg His Gln Arg Ser Val Leu Thr Asp Glu Asp Arg Lys Met Ala Glu
145                 150                 155                 160
Asn Ser Asn Lys Arg Glu Glu Asp Gln Val Glu Gly Phe Pro Glu Glu
                165                 170                 175
Val Arg Arg Ser Thr Pro Leu Ser Asp Asp Gly Glu Gly Arg Thr Asn
            180                 185                 190
Asn Asn Gly Arg Ser Met Glu Thr Ser Ser Thr His Ser Thr Arg Ile
        195                 200                 205
Thr Asp Val Ile Thr Asn Pro Ser Pro Glu Leu Glu Asp Ala Val Leu
    210                 215                 220
Gln Arg Asn Lys Arg Arg Pro Thr Thr Ile Lys Arg Asn Gln Thr Arg
225                 230                 235                 240
Ser Glu Arg Thr Gln Ser Ser Glu Leu His Lys Ser Thr Ser Glu Asn
                245                 250                 255
Ser Ser Asn Leu Glu Asp His Asn Thr Lys Thr Ser Pro Lys Val Pro
            260                 265                 270
Pro Ser Lys Asn Glu Glu Ser Ala Ala Thr Pro Lys Asn Asn His Asn
        275                 280                 285
His Arg Lys Thr Arg Tyr Thr Thr Asn Asn Ala Asn Asn Asn Thr Lys
    290                 295                 300
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Ser Pro Pro Thr Pro Glu His Asp Ala Thr Ala Asn Glu Glu Glu Thr
305 310 315 320
Ser Asn Thr Ser Val Asp Glu Met Ala Lys Leu Leu Val Ser Leu Gly
325 330 335
Val Met Lys Ser Gln His Glu Phe Glu Leu Ser Arg Ser Ala Ser His
340 345 350
Val Phe Ala Lys Arg Met Leu Lys Ser Ala Asn Tyr Lys Glu Met Thr
355 360 365
Phe Asn Leu Cys Gly Met Leu Ile Ser Val Glu Lys Ser Leu Glu Asn
370 375 380
Lys Val Glu Glu Asn Arg Thr Leu Leu Lys Gln Ile Gln Glu Glu Ile
385 390 395 400
Asn Ser Ser Arg Asp Leu His Lys Arg Phe Ser Glu Tyr Gln Lys Glu
405 410 415
Gln Asn Ser Leu Met Met Ala Asn Leu Ser Thr Leu His Ile Ile Thr
420 425 430
Asp Arg Gly Gly Lys Thr Gly Asn Pro Ser Asp Thr Thr Arg Ser Pro
435 440 445
Ser Val Phe Thr Lys Gly Lys Asp Asn Lys Val Lys Lys Thr Arg Phe
450 455 460
Asp Pro Ser Met Glu Ala Leu Gly Gly Gln Glu Phe Lys Pro Asp Leu
465 470 475 480
Ile Arg Glu Asp Glu Leu Arg Asp Asp Ile Lys Asn Pro Val Leu Glu
485 490 495
Glu Asn Asn Asn Glu Pro Gln Ala Ser Asn Ala Ser Arg Leu Ile Pro
500 505 510
Ser Thr Glu Lys His Thr Leu His Ser Leu Lys Leu Val Ile Glu Asn
515 520 525
Ser Pro Leu Ser Arg Val Glu Lys Lys Ala Tyr Ile Lys Ser Leu Tyr
530 535 540
Lys Cys Arg Thr Asn Gln Glu Val Lys Asn Val Met Glu Leu Phe Glu
545 550 555 560
Glu Asp Ile Asp Ser Leu Thr Asn
565

<210> 414
<211> 524
<212> PRT
<213> Human parainfluenza virus 1 strain Washington/1964

<220>
<223> nucleoprotein of Human parainfluenza 1 virus

<400> 414
Met Ala Gly Leu Leu Ser Thr Phe Asp Thr Phe Ser Ser Arg Arg Ser
1 5 10 15
Glu Ser Ile Asn Lys Ser Gly Gly Gly Ala Ile Ile Pro Gly Gln Arg
20 25 30
Ser Thr Val Ser Val Phe Thr Leu Gly Pro Ser Val Thr Asp Asp Ala
35 40 45
Asp Lys Leu Leu Ile Ala Thr Thr Phe Leu Ala His Ser Leu Asp Thr
50 55 60
Asp Lys Gln His Ser Gln Arg Gly Gly Phe Leu Val Ser Leu Leu Ala
65 70 75 80
Met Ala Tyr Ser Ser Pro Glu Leu Tyr Leu Thr Thr Asn Gly Val Asn
85 90 95
Ala Asp Val Lys Tyr Val Ile Tyr Asn Ile Glu Arg Asp Pro Lys Arg
100 105 110
Thr Lys Thr Asp Gly Phe Ile Val Lys Thr Arg Asp Met Glu Tyr Glu
115 120 125
Arg Thr Thr Glu Trp Leu Phe Gly Pro Met Ile Asn Lys Asn Pro Leu

```
        130                 135                 140
Phe Gln Gly Gln Arg Glu Asn Ala Asp Leu Glu Ala Leu Leu Gln Thr
145                 150                 155                 160
Tyr Gly Tyr Pro Ala Cys Leu Gly Ala Ile Ile Val Gln Val Trp Ile
                165                 170                 175
Val Leu Val Lys Ala Ile Thr Ser Ser Ala Gly Leu Arg Lys Gly Phe
            180                 185                 190
Phe Asn Arg Leu Glu Ala Phe Arg Gln Asp Gly Thr Val Lys Ser Ala
        195                 200                 205
Leu Val Phe Thr Gly Asp Thr Val Glu Gly Ile Gly Ala Val Met Arg
    210                 215                 220
Ser Gln Gln Ser Leu Val Ser Leu Met Val Glu Thr Leu Val Thr Met
225                 230                 235                 240
Asn Thr Ser Arg Ser Asp Leu Thr Thr Leu Glu Lys Asn Ile Gln Ile
                245                 250                 255
Val Gly Asn Tyr Ile Arg Asp Ala Gly Leu Ala Ser Phe Met Asn Thr
            260                 265                 270
Ile Lys Tyr Gly Val Glu Thr Lys Met Ala Ala Leu Thr Leu Ser Asn
        275                 280                 285
Leu Arg Pro Asp Ile Asn Lys Leu Arg Ser Leu Val Asp Ile Tyr Leu
    290                 295                 300
Ser Lys Gly Ala Arg Ala Pro Phe Ile Cys Ile Leu Arg Asp Pro Val
305                 310                 315                 320
His Gly Asp Phe Ala Pro Gly Asn Tyr Pro Ala Leu Trp Ser Tyr Ala
                325                 330                 335
Met Gly Val Ala Val Val Gln Asn Lys Ala Met Gln Gln Tyr Val Thr
            340                 345                 350
Gly Arg Thr Tyr Leu Asp Met Glu Met Phe Leu Leu Gly Gln Ala Val
        355                 360                 365
Ala Lys Asp Ala Asp Ser Lys Ile Ser Ser Ala Leu Glu Glu Glu Leu
    370                 375                 380
Gly Val Thr Asp Thr Ala Lys Glu Arg Leu Arg His His Leu Thr Asn
385                 390                 395                 400
Leu Ser Gly Gly Asp Gly Ala Tyr His Lys Pro Thr Gly Gly Gly Ala
                405                 410                 415
Ile Glu Val Ala Ile Asp His Thr Asp Ile Thr Phe Gly Val Glu Asp
            420                 425                 430
Thr Ala Asp Arg Asp Asn Lys Asn Trp Thr Asn Asp Ser Asn Glu Arg
        435                 440                 445
Trp Met Asn His Ser Ile Ser Asn His Thr Ile Thr Ile Arg Gly Ala
    450                 455                 460
Glu Glu Leu Glu Glu Glu Thr Asn Asp Glu Asp Ile Thr Asp Ile Glu
465                 470                 475                 480
Asn Lys Ile Ala Arg Arg Leu Ala Asp Arg Lys Gln Arg Leu Ser Gln
                485                 490                 495
Ala Asn Asn Lys Arg Asp Thr Ser Ser Asp Ala Asp Tyr Glu Asn Asp
            500                 505                 510
Asp Asp Ala Thr Ala Ala Ala Gly Ile Gly Gly Ile
        515                 520
```

<210> 415
<211> 555
<212> PRT
<213> Human parainfluenza virus 1 strain Washington/1964

<220>
<223> F glycoprotein of Human parainfluenza 1 virus

<400> 415

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Met Gln Lys Ser Glu Ile Leu Phe Leu Val Tyr Ser Ser Leu Leu Leu
 1               5                  10                  15
```

Ser Ser Ser Leu Cys Gln Ile Pro Val Glu Lys Leu Ser Asn Val Gly
20 25 30
Val Ile Ile Asn Glu Gly Lys Leu Leu Lys Ile Ala Gly Ser Tyr Glu
35 40 45
Ser Arg Tyr Ile Val Leu Ser Leu Val Pro Ser Ile Asp Leu Gln Asp
50 55 60
Gly Cys Gly Thr Thr Gln Ile Ile Gln Tyr Lys Asn Leu Leu Asn Arg
65 70 75 80
Leu Leu Ile Pro Leu Lys Asp Ala Leu Asp Leu Gln Glu Ser Leu Ile
85 90 95
Thr Ile Thr Asn Asp Thr Thr Val Thr Asn Asp Asn Pro Gln Thr Arg
100 105 110
Phe Phe Gly Ala Val Ile Gly Thr Ile Ala Leu Gly Val Ala Thr Ala
115 120 125
Ala Gln Ile Thr Ala Gly Ile Ala Leu Ala Glu Ala Arg Glu Ala Arg
130 135 140
Lys Asp Ile Ala Leu Ile Lys Asp Ser Ile Val Lys Thr His Asn Ser
145 150 155 160
Val Glu Leu Ile Gln Arg Gly Ile Gly Glu Gln Ile Ile Ala Leu Lys
165 170 175
Thr Leu Gln Asp Phe Val Asn Asp Glu Ile Arg Pro Ala Ile Gly Glu
180 185 190
Leu Arg Cys Glu Thr Thr Ala Leu Lys Leu Gly Ile Lys Leu Thr Gln
195 200 205
His Tyr Ser Glu Leu Ala Thr Ala Phe Ser Ser Asn Leu Gly Thr Ile
210 215 220
Gly Glu Lys Ser Leu Thr Leu Gln Ala Leu Ser Ser Leu Tyr Ser Ala
225 230 235 240
Asn Ile Thr Glu Ile Leu Ser Thr Thr Lys Lys Asp Lys Ser Asp Ile
245 250 255
Tyr Asp Ile Ile Tyr Thr Glu Gln Val Lys Gly Thr Val Ile Asp Val
260 265 270
Asp Leu Glu Lys Tyr Met Val Thr Leu Leu Val Lys Ile Pro Ile Leu
275 280 285
Ser Glu Ile Pro Gly Val Leu Ile Tyr Arg Ala Ser Ser Ile Ser Tyr
290 295 300
Asn Ile Glu Gly Glu Glu Trp His Val Ala Ile Pro Asn Tyr Ile Ile
305 310 315 320
Asn Lys Ala Ser Ser Leu Gly Gly Ala Asp Val Thr Asn Cys Ile Glu
325 330 335
Ser Lys Leu Ala Tyr Ile Cys Pro Arg Asp Pro Thr Gln Leu Ile Pro
340 345 350
Asp Asn Gln Gln Lys Cys Ile Leu Gly Asp Val Ser Lys Cys Pro Val
355 360 365
Thr Lys Val Ile Asn Asn Leu Val Pro Lys Phe Ala Phe Ile Asn Gly
370 375 380
Gly Val Val Ala Asn Cys Ile Ala Ser Thr Cys Thr Cys Gly Thr Asn
385 390 395 400
Arg Ile Pro Val Asn Gln Asp Arg Ser Arg Gly Val Thr Phe Leu Thr
405 410 415
Tyr Thr Asn Cys Gly Leu Ile Gly Ile Asn Gly Ile Glu Leu Tyr Ala
420 425 430
Asn Lys Arg Gly Arg Asp Thr Thr Trp Gly Asn Gln Ile Ile Lys Val
435 440 445
Gly Pro Ala Val Ser Ile Arg Pro Val Asp Ile Ser Leu Asn Leu Ala
450 455 460
Ser Ala Thr Asn Phe Leu Glu Glu Ser Lys Thr Glu Leu Met Lys Ala
465 470 475 480
Arg Ala Ile Ile Ser Ala Val Gly Gly Trp His Asn Thr Glu Ser Thr
485 490 495
Gln Ile Ile Met Ile Ile Ile Val Cys Ile Leu Ile Ile Ile Ile Cys

500 505 510
Gly Ile Leu Tyr Tyr Leu Tyr Arg Val Arg Arg Leu Leu Val Met Ile
515 520 525
Asn Ser Thr His Asn Ser Pro Val Asn Ala Tyr Thr Leu Glu Ser Arg
530 535 540
Met Arg Asn Pro Tyr Met Gly Asn Asn Ser Asn
545 550 555

<210> 416
<211> 373
<212> PRT
<213> Human parainfluenza virus 3

<220>
<223> D protein of Human parainfluenza virus 3

<400> 416
Met Glu Ser Asp Ala Lys Asn Tyr Gln Ile Met Asp Ser Trp Glu Glu
1 5 10 15
Glu Ser Arg Asp Lys Ser Thr Asn Ile Ser Ser Ala Leu Asn Ile Ile
20 25 30
Glu Phe Ile Leu Ser Thr Asp Pro Gln Glu Asp Leu Ser Glu Asn Asp
35 40 45
Thr Ile Asn Thr Arg Thr Gln Gln Leu Ser Ala Thr Ile Tyr Gln Pro
50 55 60
Lys Ile Lys Pro Thr Glu Thr Ser Glu Lys Asp Ser Gly Ser Thr Asp
65 70 75 80
Lys Asn Arg Gln Ser Gly Ser Ser His Glu Cys Thr Thr Glu Ala Lys
85 90 95
Asp Arg Thr Ile Asp Gln Glu Thr Val Gln Arg Gly Pro Gly Arg Arg
100 105 110
Ser Ser Ser Asp Ser Arg Ala Glu Thr Val Val Ser Gly Gly Ile Ser
115 120 125
Arg Ser Ile Thr Asn Ser Lys Asn Gly Thr Gln Asn Thr Glu Asp Ile
130 135 140
Asp Leu Asn Glu Ile Arg Lys Met Asp Lys Asp Ser Ile Glu Gly Lys
145 150 155 160
Val Arg Gln Ser Ala Asp Val Pro Ser Glu Ile Ser Gly Ser Asp Val
165 170 175
Ile Phe Thr Thr Glu Gln Ser Arg Asn Ser Asp His Gly Arg Ser Leu
180 185 190
Glu Ser Ile Ser Thr Pro Asp Thr Arg Ser Ile Ser Val Val Thr Ala
195 200 205
Ala Thr Pro Asp Asp Glu Glu Glu Ile Leu Met Lys Asn Ser Arg Thr
210 215 220
Lys Lys Ser Ser Ser Ile His Gln Glu Asp Asp Lys Arg Ile Lys Lys
225 230 235 240
Gly Gly Glu Lys Gly Lys Thr Gly Leu Arg Asn Gln Lys Ile Leu Thr
245 250 255
Thr Arg Tyr Gln His Gln Thr Thr Asp Pro His Gln Lys Gly Arg Arg
260 265 270
Lys Ser Gln Lys Gln Gln Pro Ser Thr Pro Thr Gln Arg Gly Lys Gln
275 280 285
Lys Tyr Arg Gln Asn His Gln Glu His Asn Pro His His Gly Ile Ser
290 295 300
Pro Leu Ile Thr Thr Gln Ile Glu Pro Asn Arg Gln Thr Gln Leu Pro
305 310 315 320
Gln Gln Gln Pro Pro Asp Gln Leu Ile Gln Lys Asn Gln Ser Glu Gln
325 330 335
Thr Leu Asp Pro Asn Pro Arg His Lys Arg Gln Met Glu Arg Lys Gly
340 345 350

Arg Ile Gln Lys Arg Ala Ile Asp Leu Gln Arg Gly Gln Leu Leu Tyr
355 360 365
Cys Arg Ile Leu Val
370

<210> 417
<211> 574
<212> PRT
<213> Human parainfluenza virus 3

<220>
<223> hemagglutinin-neuraminidase of Human parainfluenza virus 3

<400> 417
Met Glu Tyr Trp Lys His Thr Asn His Gly Lys Asp Ala Gly Asn Glu
1 5 10 15
Leu Glu Thr Ser Met Ala Thr His Asn Asn Lys Leu Thr Asn Lys Ile
20 25 30
Ile Tyr Ile Leu Trp Thr Ile Ile Leu Val Leu Leu Ser Ile Val Phe
35 40 45
Ile Ile Val Leu Ile Asn Ser Ile Asn Ser Glu Lys Val His Asn Ser
50 55 60
Leu Leu Gln Glu Ile Asn Asn Glu Phe Met Glu Ile Thr Glu Lys Ile
65 70 75 80
Gln Met Ala Ser Asp Asn Thr Asn Asp Leu Ile Gln Ser Gly Val Asn
85 90 95
Thr Arg Leu Leu Thr Ile Gln Ser His Val Gln Asn Tyr Ile Pro Ile
100 105 110
Ser Leu Thr Gln Gln Met Ser Asp Leu Arg Lys Phe Ile Ser Glu Ile
115 120 125
Thr Ile Arg Asn Asp Asn Gln Glu Val Pro Gln Gln Arg Ile Thr His
130 135 140
Asp Val Gly Ile Lys Pro Leu Asn Pro Asp Asp Phe Trp Arg Cys Thr
145 150 155 160
Ser Gly Leu Pro Phe Leu Met Arg Asn Pro Lys Ile Arg Leu Met Pro
165 170 175
Gly Pro Gly Leu Leu Ala Met Pro Thr Thr Val Asp Gly Cys Val Arg
180 185 190
Thr Pro Ser Leu Ile Ile Asn Asp Leu Ile Tyr Ala Tyr Thr Ser Asn
195 200 205
Leu Ile Thr Arg Gly Cys Gln Asp Ile Gly Lys Ser Tyr Gln Val Leu
210 215 220
Gln Val Gly Ile Ile Thr Val Asn Ser Asp Leu Val Pro Asp Leu Asn
225 230 235 240
Pro Arg Phe Ser His Thr Phe Asn Ile Asn Asp Asn Arg Lys Ser Cys
245 250 255
Ser Leu Ala Leu Leu Asn Thr Asp Val Tyr Gln Leu Cys Ser Thr Pro
260 265 270
Lys Val Asp Glu Arg Ser Asp Tyr Ala Ser Ser Gly Ile Glu Asp Ile
275 280 285
Val Leu Asp Ile Val Asn Tyr Asp Gly Ser Ile Ser Thr Thr Arg Phe
290 295 300
Lys Asn Asn Asn Ile Ser Phe Asp Gln Pro Tyr Ala Ala Leu Tyr Pro
305 310 315 320
Ser Val Gly Pro Gly Ile Tyr Tyr Lys Gly Lys Ile Ile Phe Leu Gly
325 330 335
Tyr Gly Gly Leu Glu His Pro Ile Asn Glu Asn Val Ile Cys Asn Thr
340 345 350
Thr Glu Cys Pro Gly Lys Thr Gln Arg Asp Cys Asn Gln Ala Ser Tyr
355 360 365
Ser Pro Trp Phe Ser Asp Arg Arg Met Val Asn Ser Ile Ile Val Val

370 375 380
Asp Lys Gly Leu Asn Ser Ile Pro Lys Leu Lys Val Trp Thr Ile Ser
385 390 395 400
Met Arg Gln Asn Tyr Trp Gly Ser Glu Gly Arg Leu Ile Leu Leu Gly
405 410 415
Asn Lys Ile Tyr Ile Tyr Thr Arg Ser Thr Ser Trp His Ser Lys Leu
420 425 430
Gln Leu Gly Ile Ile Asp Ile Thr Asp Tyr Ser Asp Ile Arg Ile Lys
435 440 445
Trp Thr Trp His Asn Val Leu Ser Arg Pro Gly Asn Asp Glu Cys Pro
450 455 460
Trp Gly His Ser Cys Pro Asn Gly Cys Ile Thr Gly Val Tyr Thr Asp
465 470 475 480
Ala Tyr Pro Leu Asn Pro Thr Gly Ser Ile Val Ser Ser Val Ile Leu
485 490 495
Asp Ser Gln Lys Ser Arg Val Asn Pro Val Ile Thr Tyr Ser Thr Ala
500 505 510
Thr Glu Arg Val Asn Glu Leu Ala Ile Arg Asn Arg Thr Leu Ser Ala
515 520 525
Gly Tyr Thr Thr Thr Ser Cys Ile Thr His Tyr Asp Lys Gly Tyr Cys
530 535 540
Phe His Ile Val Glu Ile Asn Gln Lys Ser Ser Asn Thr Phe Gln Pro
545 550 555 560
Met Leu Phe Lys Thr Glu Ile Pro Lys Ser Cys Ser Gln Ser
565 570

<210> 418
<211> 515
<212> PRT
<213> Human parainfluenza virus 3

<220>
<223> nucleocapsid protein of Human parainfluenza virus 3

<400> 418
Met Leu Ser Leu Phe Asp Thr Phe Asn Ala Arg Arg Gln Glu Asn Ile
1 5 10 15
Thr Lys Ser Ala Gly Gly Ala Ile Ile Pro Gly Gln Lys Asn Thr Val
20 25 30
Ser Ile Phe Ala Leu Gly Pro Thr Ile Thr Asp Asp Asn Glu Lys Met
35 40 45
Thr Leu Ala Leu Leu Phe Leu Ser His Ser Leu Asp Asn Glu Lys Gln
50 55 60
His Ala Gln Arg Ala Gly Phe Leu Val Ser Leu Leu Ser Met Ala Tyr
65 70 75 80
Ala Asn Pro Glu Leu Tyr Leu Thr Thr Asn Gly Ser Asn Ala Asp Val
85 90 95
Lys Tyr Val Ile Tyr Met Ile Glu Lys Asp Leu Lys Arg Gln Lys Tyr
100 105 110
Gly Gly Phe Val Val Lys Thr Arg Glu Met Val Tyr Asp Lys Thr Thr
115 120 125
Asp Trp Ile Phe Gly Ser Asp Leu Asp Cys Asp Gln Glu Thr Met Leu
130 135 140
Gln Asn Gly Arg Asn Asn Ser Thr Ile Glu Asp Leu Val His Thr Phe
145 150 155 160
Gly Tyr Pro Ser Cys Leu Gly Ala Leu Ile Ile Gln Ile Trp Ile Val
165 170 175
Leu Val Lys Ala Ile Thr Ser Ile Ser Gly Leu Arg Lys Gly Phe Phe
180 185 190
Thr Arg Leu Glu Ala Phe Arg Gln Asp Gly Thr Val Gln Ala Gly Leu

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        195                     200                     205
Val Leu Ser Gly Asp Thr Val Asp Gln Ile Gly Ser Ile Met Arg Ser
    210                     215                     220
Gln Gln Ser Leu Val Thr Leu Met Val Glu Thr Leu Ile Thr Met Asn
225                     230                     235                     240
Thr Ser Arg Asn Asp Leu Thr Thr Ile Glu Lys Asn Ile Gln Ile Val
                245                     250                     255
Gly Asn Tyr Ile Arg Asp Ala Gly Leu Ala Ser Phe Phe Asn Thr Ile
            260                     265                     270
Arg Tyr Gly Ile Glu Thr Arg Met Ala Ala Leu Thr Leu Ser Thr Leu
        275                     280                     285
Arg Pro Asp Ile Asn Arg Leu Lys Ala Leu Met Glu Leu Tyr Leu Ser
    290                     295                     300
Lys Gly Pro Arg Ala Pro Phe Ile Cys Ile Leu Arg Asp Pro Ile His
305                     310                     315                     320
Gly Glu Phe Ala Pro Gly Asn Tyr Pro Ala Ile Trp Ser Tyr Ala Met
                325                     330                     335
Gly Val Ala Val Val Gln Asn Arg Ala Met Gln Gln Tyr Val Thr Gly
            340                     345                     350
Arg Ser Tyr Leu Asp Ile Asp Met Phe Gln Leu Gly Gln Ala Val Ala
        355                     360                     365
Arg Asp Ala Glu Ala Gln Met Ser Ser Thr Leu Glu Asp Glu Leu Gly
    370                     375                     380
Val Thr His Glu Ala Lys Glu Ser Leu Lys Arg His Ile Arg Asn Ile
385                     390                     395                     400
Asn Ser Ser Glu Thr Ser Phe His Lys Pro Thr Gly Gly Ser Ala Ile
                405                     410                     415
Glu Met Ala Ile Asp Glu Glu Pro Glu Gln Phe Glu His Arg Ser Asp
            420                     425                     430
Gln Glu Arg Asp Gly Glu Pro Gln Ser Ser Ile Ile Gln Tyr Ala Trp
        435                     440                     445
Ala Glu Gly Asn Arg Ser Asp Asp Arg Thr Glu Gln Asp Thr Glu Ser
    450                     455                     460
Asp Asn Ile Lys Thr Glu Gln Gln Asn Ile Arg Asp Arg Leu Asn Lys
465                     470                     475                     480
Arg Leu Asn Glu Lys Lys Lys Gln Gly Ser Gln Pro Pro Thr Asn Pro
                485                     490                     495
Thr Asn Arg Thr Asn Gln Asp Glu Ile Asp Asp Leu Phe Asn Ala Phe
            500                     505                     510
Gly Ser Asn
        515


<210> 419
<211> 395
<212> PRT
<213> Human parainfluenza virus 2

<220>
<223>   P protein of Human parainfluenza virus 2

<400> 419
Met Ala Glu Glu Pro Thr Tyr Thr Thr Glu Gln Val Asp Glu Leu Ile
1               5                   10                  15
His Ala Gly Leu Gly Thr Val Asp Phe Phe Leu Ser Arg Pro Ile Asp
            20                  25                  30
Ala Gln Ser Ser Leu Gly Lys Gly Ser Ile Pro Pro Gly Val Thr Ala
        35                  40                  45
Val Leu Thr Ser Ala Ala Glu Thr Lys Ser Lys Pro Val Ala Ala Gly
    50                  55                  60
Pro Val Lys Pro Arg Arg Lys Lys Val Ile Ser Asn Thr Thr Pro Tyr
```

65 70 75 80
Thr Ile Ala Asp Asn Ile Pro Pro Glu Lys Leu Pro Ile Asn Thr Pro
85 90 95
Ile Pro Asn Pro Leu Leu Pro Leu Ala Arg Pro His Gly Lys Met Thr
100 105 110
Asp Ile Asp Ile Val Thr Gly Asn Ile Thr Glu Gly Ser Tyr Lys Gly
115 120 125
Val Glu Leu Ala Lys Leu Gly Lys Gln Thr Leu Leu Thr Arg Phe Thr
130 135 140
Ser Asn Glu Pro Val Ser Ser Ala Gly Ser Ala Gln Asp Pro Asn Phe
145 150 155 160
Lys Arg Gly Gly Glu Leu Ile Glu Lys Glu Gln Glu Ala Thr Ile Gly
165 170 175
Glu Asn Gly Val Leu His Gly Ser Glu Ile Arg Ser Lys Ser Ser Ser
180 185 190
Gly Val Ile Pro Gly Val Pro Gln Ser Arg Pro Gln Leu Ala Ser Ser
195 200 205
Pro Ala His Ala Asp Pro Ala Pro Ala Ser Ala Glu Asn Val Lys Glu
210 215 220
Ile Ile Glu Leu Leu Lys Gly Leu Asp Leu Arg Leu Gln Thr Val Glu
225 230 235 240
Gly Lys Val Asp Lys Ile Leu Ala Thr Ser Ala Thr Ile Ile Asn Leu
245 250 255
Lys Asn Glu Met Thr Ser Leu Lys Ala Ser Val Ala Thr Met Glu Gly
260 265 270
Met Ile Thr Thr Ile Lys Ile Met Asp Pro Ser Thr Pro Thr Asn Val
275 280 285
Pro Val Glu Glu Ile Arg Lys Ser Leu His Asn Val Pro Val Val Ile
290 295 300
Ala Gly Pro Thr Ser Gly Gly Phe Thr Ala Glu Gln Val Ile Leu Ile
305 310 315 320
Ser Met Asp Glu Leu Ala Arg Pro Thr Leu Ser Ser Thr Lys Arg Ile
325 330 335
Thr Arg Lys Pro Glu Ser Lys Lys Asp Leu Thr Gly Ile Lys Leu Thr
340 345 350
Leu Met Gln Leu Ala Asn Asp Cys Ile Ser Arg Pro Asp Thr Lys Thr
355 360 365
Glu Phe Val Thr Lys Ile Gln Ala Ala Thr Thr Glu Ser Gln Leu Asn
370 375 380
Glu Ile Lys Arg Ser Ile Ile Arg Ser Ala Ile
385 390 395

<210> 420
<211> 539
<212> PRT
<213> Human parainfluenza virus

<220>
<223> F protein of Human parainfluenza virus

<400> 420
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1 5 10 15
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30
Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ala Asp Gly Pro
50 55 60
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu

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65                  70                  75                  80
Leu Arg Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95
Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125
Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Lys Thr
    130                 135                 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175
Ile Asn Lys Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser
            180                 185                 190
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220
Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240
Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255
Gly Phe Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285
Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335
Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350
Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445
Val Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460
Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480
Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
                485                 490                 495
Leu Ile Ala Val Leu Gly Ser Thr Met Ile Leu Val Ser Val Phe Ile
            500                 505                 510
Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
        515                 520                 525
Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn
    530                 535
```

<210> 421
<211> 236
<212> PRT
<213> Human parainfluenza virus

<220>
<223> G protein of Human parainfluenza virus

<400> 421
Met Glu Val Lys Val Glu Asn Ile Arg Thr Ile Asp Met Leu Lys Ala
1 5 10 15
Arg Val Lys Asn Arg Val Ala Arg Ser Lys Cys Phe Lys Asn Ala Ser
20 25 30
Leu Val Leu Ile Gly Ile Thr Thr Leu Ser Ile Ala Leu Asn Ile Tyr
35 40 45
Leu Ile Ile Asn Tyr Lys Met Gln Lys Asn Thr Ser Glu Ser Glu His
50 55 60
His Thr Ser Ser Ser Pro Met Glu Ser Ser Arg Glu Thr Pro Thr Val
65 70 75 80
Pro Thr Asp Asn Ser Asp Thr Asn Ser Ser Pro Gln His Pro Thr Gln
85 90 95
Gln Ser Thr Glu Gly Ser Thr Leu Tyr Phe Ala Ala Ser Ala Ser Ser
100 105 110
Pro Glu Thr Glu Pro Thr Ser Thr Pro Asp Thr Thr Asn Arg Pro Pro
115 120 125
Phe Val Asp Thr His Thr Thr Pro Pro Ser Ala Ser Arg Thr Lys Thr
130 135 140
Ser Pro Ala Val His Thr Lys Asn Asn Pro Arg Thr Ser Ser Arg Thr
145 150 155 160
His Ser Pro Pro Arg Ala Thr Thr Arg Thr Ala Arg Arg Thr Thr Thr
165 170 175
Leu Arg Thr Ser Ser Thr Arg Lys Arg Pro Ser Thr Ala Ser Val Gln
180 185 190
Pro Asp Ile Ser Ala Thr Thr His Lys Asn Glu Glu Ala Ser Pro Ala
195 200 205
Ser Pro Gln Thr Ser Ala Ser Thr Thr Arg Ile Gln Arg Lys Ser Val
210 215 220
Glu Ala Asn Thr Ser Thr Thr Tyr Asn Gln Thr Ser
225 230 235

<210> 422
<211> 120
<212> PRT
<213> Homo sapiens

<400> 422
Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ala
20 25 30
Gly Met Ser Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45
Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys His Tyr Asn Pro Ser
50 55 60
Leu Lys Asp Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80
Val Leu Lys Val Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr
85 90 95
Cys Ala Arg Asp Met Ile Phe Asn Phe Tyr Phe Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 423
<211> 106
<212> PRT
<213> Homo sapiens

<400> 423
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Arg Val Gly Tyr Met
20 25 30
His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45
Asp Thr Leu Leu Leu Asp Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp
65 70 75 80
Asp Phe Ala Thr Tyr Tyr Cys Phe Gln Gly Ser Gly Tyr Pro Phe Thr
85 90 95
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 424
<211> 532
<212> PRT
<213> Avian pneumovirus

<220>
<223> Avian pneumovirus fusion protein gene

<400> 424
Met Ser Trp Lys Val Val Leu Leu Leu Val Leu Leu Ala Thr Pro Thr
1 5 10 15
Gly Gly Leu Glu Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Val Thr
20 25 30
Arg Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Gly Val Gly Asp Val Lys Asn Leu Thr Cys Thr Asp Gly Pro
50 55 60
Ser Leu Ile Arg Thr Glu Leu Glu Leu Thr Lys Asn Ala Leu Glu Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Lys Glu Ala Arg Ile Met
85 90 95
Ser Pro Arg Lys Ala Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Gly Glu Val Ala Ala Ile Lys Gly Ala Leu Arg Lys Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160
Ala Val Asn Asp Leu Lys Asp Phe Ile Ser Lys Lys Leu Thr Pro Ala
165 170 175
Ile Asn Arg Asn Lys Cys Asp Ile Ser Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Gly Gln Tyr Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Val Arg Ala Val Ser Asn Met Pro Thr Ser Ser Gly Gln
225 230 235 240
Ile Asn Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Val Tyr Ile Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Arg Val Lys Ala
275 280 285
Ala Pro Leu Cys Ser Gly Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Glu Asp Cys Glu Val Arg Ser Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Lys Glu Ser Glu Glu Cys Asn Arg
340 345 350
Asn Ile Ser Thr Thr Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Asp Gly Met Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385 390 395 400
Arg Pro Leu Gly Lys Gly Cys Ser Tyr Ile Ser Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Thr Ile Lys Gly Lys Pro Val Ser Ser Asn Phe Asp Pro
435 440 445
Ile Glu Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Val Glu Lys Ser Gln Asn Leu Ile Asp Gln Ser Asn Lys Ile
465 470 475 480
Leu Asp Ser Ile Glu Lys Gly Asn Ala Gly Phe Val Ile Val Ile Val
485 490 495
Leu Ile Val Leu Leu Met Leu Ala Ala Val Gly Val Gly Val Phe Phe
500 505 510
Val Val Lys Lys Arg Lys Ala Ala Pro Lys Phe Pro Met Glu Met Asn
515 520 525
Gly Val Asn Asn
530

<210> 425
<211> 537
<212> PRT
<213> Avian pneumovirus

<220>
<223> Avian pneumovirus isolate 1b fusion protein mRNA

<400> 425
Met Ser Trp Lys Val Val Leu Leu Leu Val Leu Leu Ala Thr Pro Thr
1 5 10 15
Gly Gly Leu Glu Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Val Thr
20 25 30
Arg Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
50 55 60

Ser Leu Ile Arg Thr Glu Leu Glu Leu Thr Lys Asn Ala Leu Glu Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Lys Glu Ala Arg Ile Met
85 90 95
Ser Pro Arg Lys Ala Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Gly Glu Val Ala Ala Ile Lys Gly Ala Leu Arg Lys Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160
Ala Val Asn Asp Leu Lys Asp Phe Ile Ser Lys Lys Leu Thr Pro Ala
165 170 175
Ile Asn Arg Asn Lys Cys Asp Ile Ser Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Gly Gln Tyr Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Val Arg Ala Val Ser Asn Met Pro Thr Ser Ser Gly Gln
225 230 235 240
Ile Asn Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Val Tyr Ile Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Lys Val Lys Ala
275 280 285
Ala Pro Leu Cys Ser Gly Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Glu Asp Cys Glu Val Arg Ser Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Lys Glu Ser Glu Glu Cys Asn Arg
340 345 350
Asn Ile Ser Thr Thr Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Asp Gly Met Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385 390 395 400
Arg Pro Leu Gly Lys Gly Cys Ser Tyr Ile Ser Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Thr Ile Lys Gly Lys Pro Val Ser Ser Asn Phe Asp Pro
435 440 445
Ile Glu Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Val Glu Lys Ser Gln Asn Leu Ile Asp Gln Ser Asn Lys Ile
465 470 475 480
Leu Asp Ser Ile Glu Lys Gly Asn Ala Gly Phe Val Ile Val Ile Val
485 490 495
Leu Ile Val Leu Leu Met Leu Ala Ala Val Gly Val Gly Val Phe Phe
500 505 510
Val Val Lys Lys Arg Lys Ala Ala Pro Lys Phe Pro Met Glu Met Asn
515 520 525
Gly Val Asn Asn Lys Gly Phe Ile Pro
530 535

<210> 426
<211> 538
<212> PRT
<213> Turkey rhinotracheitis virus

<220>
<223> Turkey rhinotracheitis virus gene for fusion
protein (F1 and F2 subunits), complete cds

<400> 426
Met Asp Val Arg Ile Cys Leu Leu Leu Phe Leu Ile Ser Asn Pro Ser
1 5 10 15
Ser Cys Ile Gln Glu Thr Tyr Asn Glu Glu Ser Cys Ser Thr Val Thr
20 25 30
Arg Gly Tyr Lys Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Asn Leu Glu Ile Gly Asn Val Glu Asn Ile Thr Cys Asn Asp Gly Pro
50 55 60
Ser Leu Ile Asp Thr Glu Leu Val Leu Thr Lys Asn Ala Leu Arg Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Val Ala Lys Glu Ser Arg Leu Ser
85 90 95
Ser Pro Arg Arg Arg Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Leu Ala Lys Thr Ile
115 120 125
Arg Leu Glu Gly Glu Val Lys Ala Ile Lys Asn Ala Leu Arg Asn Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160
Ala Val Asn Asp Leu Lys Glu Phe Ile Ser Lys Lys Leu Thr Pro Ala
165 170 175
Ile Asn Gln Asn Lys Cys Asn Ile Ala Asp Ile Lys Met Ala Ile Ser
180 185 190
Phe Gly Gln Asn Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Ser Ala Gly Ile Thr Ser Ala Val Ser Leu Asp Leu Met Thr Asp
210 215 220
Asp Glu Leu Val Arg Ala Ile Asn Arg Met Pro Thr Ser Ser Gly Gln
225 230 235 240
Ile Ser Leu Met Leu Asn Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255
Gly Ile Leu Ile Gly Val Tyr Asp Gly Thr Val Val Tyr Met Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Glu Thr Pro Cys Trp Arg Val Val Ala
275 280 285
Ala Pro Leu Cys Arg Lys Glu Lys Gly Asn Tyr Ala Cys Ile Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Thr Asn Ala Gly Ser Thr Ala Tyr Tyr
305 310 315 320
Pro Asn Lys Asp Asp Cys Glu Val Arg Asp Asp Tyr Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Leu Glu Val Glu Gln Cys Asn Tyr
340 345 350
Asn Ile Ser Thr Ser Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Val Ser Met Val Ala Leu Thr Pro Leu Gly Gly Leu Val Ser Cys
370 375 380
Tyr Glu Ser Val Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385 390 395 400
Lys Gln Leu Gly Lys Gly Cys Thr His Ile Pro Asn Asn Glu Ala Asp

405 410 415
Thr Ile Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Val Gly
420 425 430
Glu Gln Arg Thr Ile Lys Gly Ala Pro Val Val Asn Asn Phe Asn Pro
435 440 445
Ile Leu Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Ile Asp Arg Ser Gln Asp Leu Ile Asp Lys Ser Asn Asp Leu
465 470 475 480
Leu Gly Ala Asp Ala Lys Ser Lys Ala Gly Ile Ala Ile Ala Ile Val
485 490 495
Val Leu Val Ile Leu Gly Ile Phe Phe Leu Leu Ala Val Ile Tyr Tyr
500 505 510
Cys Ser Arg Val Arg Lys Thr Lys Pro Lys His Asp Tyr Pro Ala Thr
515 520 525
Thr Gly His Ser Ser Met Ala Tyr Val Ser
530 535

<210> 427
<211> 537
<212> PRT
<213> Avian penumovirus

<220>
<223> Avian pneumovirus fusion glycoprotein (F) gene,
complete cds

<400> 427
Met Ser Trp Lys Val Val Leu Leu Leu Val Leu Leu Ala Thr Pro Thr
1 5 10 15
Gly Gly Leu Glu Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Val Thr
20 25 30
Arg Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45
Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro
50 55 60
Ser Leu Ile Arg Thr Glu Leu Glu Leu Thr Lys Asn Ala Leu Glu Glu
65 70 75 80
Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Lys Glu Ala Arg Ile Met
85 90 95
Ser Pro Arg Lys Ala Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110
Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
115 120 125
Arg Leu Glu Gly Glu Val Ala Ala Ile Lys Gly Ala Leu Arg Lys Thr
130 135 140
Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145 150 155 160
Ala Val Asn Asp Leu Lys Asp Phe Ile Ser Lys Lys Leu Thr Pro Ala
165 170 175
Ile Asn Arg Asn Lys Cys Asp Ile Ser Asp Leu Lys Met Ala Val Ser
180 185 190
Phe Gly Gln Tyr Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
195 200 205
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
210 215 220
Ala Glu Leu Val Arg Ala Val Ser Asn Met Pro Thr Ser Ser Gly Gln
225 230 235 240
Ile Asn Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
245 250 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Val Tyr Ile Val Gln
260 265 270
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Lys Val Lys Ala
275 280 285
Ala Pro Leu Cys Ser Gly Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg
290 295 300
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305 310 315 320
Pro Asn Glu Glu Asp Cys Glu Val Arg Ser Asp His Val Phe Cys Asp
325 330 335
Thr Ala Ala Gly Ile Asn Val Ala Lys Glu Ser Glu Glu Cys Asn Arg
340 345 350
Asn Ile Ser Thr Thr Lys Tyr Pro Cys Lys Val Ser Thr Gly Arg His
355 360 365
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
370 375 380
Tyr Asp Gly Met Ser Cys Ser Ile Gly Ser Asn Lys Val Gly Ile Ile
385 390 395 400
Arg Pro Leu Gly Lys Gly Cys Ser Tyr Ile Ser Asn Gln Asp Ala Asp
405 410 415
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
420 425 430
Glu Gln His Thr Ile Lys Gly Lys Pro Val Ser Ser Asn Phe Asp Pro
435 440 445
Ile Glu Phe Pro Glu Asp Gln Phe Asn Ile Ala Leu Asp Gln Val Phe
450 455 460
Glu Ser Val Glu Lys Ser Gln Asn Leu Ile Asp Gln Ser Asn Lys Ile
465 470 475 480
Leu Asp Ser Ile Glu Lys Gly Asn Ala Gly Phe Val Ile Val Ile Val
485 490 495
Leu Ile Val Leu Leu Met Leu Ala Ala Val Gly Val Gly Val Phe Phe
500 505 510
Val Val Lys Lys Arg Lys Ala Ala Pro Lys Phe Pro Met Glu Met Asn
515 520 525
Gly Val Asn Asn Lys Gly Phe Ile Pro
530 535

<210> 428
<211> 391
<212> PRT
<213> Turkey rhinotracheitis virus

<220>
<223> Turkey rhinotracheitis virus (strain CVL14/1)
attachment protien (G) mRNA, complete cds

<400> 428
Met Gly Ser Lys Leu Tyr Met Ala Gln Gly Thr Ser Ala Tyr Gln Thr
1 5 10 15
Ala Val Gly Phe Trp Leu Asp Ile Gly Arg Arg Tyr Ile Leu Ala Ile
20 25 30
Val Leu Ser Ala Phe Gly Leu Thr Cys Thr Val Thr Ile Ala Leu Thr
35 40 45
Val Ser Val Ile Val Glu Gln Ser Val Leu Glu Glu Cys Arg Asn Tyr
50 55 60
Asn Gly Gly Asp Arg Asp Trp Trp Ser Thr Thr Gln Glu Gln Pro Thr
65 70 75 80
Thr Ala Pro Ser Ala Thr Pro Ala Gly Asn Tyr Gly Gly Leu Gln Thr
85 90 95
Ala Arg Thr Arg Lys Ser Glu Ser Cys Leu His Val Gln Ile Ser Tyr

```
                100                     105                     110
Gly Asp Met Tyr Ser Arg Ser Asp Thr Val Leu Gly Gly Phe Asp Cys
        115                     120                     125
Met Gly Leu Leu Val Leu Cys Lys Ser Gly Pro Ile Cys Gln Arg Asp
    130                     135                     140
Asn Gln Val Asp Pro Thr Ala Leu Cys His Cys Arg Val Asp Leu Ser
145                     150                     155                     160
Ser Val Asp Cys Cys Lys Val Asn Lys Ile Ser Thr Asn Ser Ser Thr
                    165                     170                     175
Thr Ser Glu Pro Gln Lys Thr Asn Pro Ala Trp Pro Ser Gln Asp Asn
                180                     185                     190
Thr Asp Ser Asp Pro Asn Pro Gln Gly Ile Thr Thr Ser Thr Ala Thr
        195                     200                     205
Leu Leu Ser Thr Ser Leu Gly Leu Met Leu Thr Ser Lys Thr Gly Thr
    210                     215                     220
His Lys Ser Gly Pro Pro Gln Ala Leu Pro Gly Ser Asn Thr Asn Gly
225                     230                     235                     240
Lys Thr Thr Thr Asp Arg Glu Pro Gly Pro Thr Asn Gln Pro Asn Ser
                    245                     250                     255
Thr Thr Asn Gly Gln His Asn Lys His Thr Gln Arg Met Thr Pro Pro
                260                     265                     270
Pro Ser His Asp Asn Thr Arg Thr Ile Leu Gln His Thr Thr Pro Trp
        275                     280                     285
Glu Lys Thr Phe Ser Thr Tyr Lys Pro Thr His Ser Pro Thr Asn Glu
    290                     295                     300
Ser Asp Gln Ser Leu Pro Thr Thr Gln Asn Ser Ile Asn Cys Glu His
305                     310                     315                     320
Phe Asp Pro Gln Gly Lys Glu Lys Ile Cys Tyr Arg Val Gly Ser Tyr
                    325                     330                     335
Asn Ser Asn Ile Thr Lys Gln Cys Arg Ile Asp Val Pro Leu Cys Ser
                340                     345                     350
Thr Tyr Ser Thr Val Cys Met Lys Thr Tyr Tyr Thr Glu Pro Phe Asn
        355                     360                     365
Cys Trp Arg Arg Ile Trp Arg Cys Leu Cys Asp Asp Gly Val Gly Leu
    370                     375                     380
Val Glu Trp Cys Cys Thr Ser
385                     390

<210> 429
<211> 414
<212> PRT
<213> rhinotracheitis virus

<220>
<223> Turkey rhinotracheitis virus (strain 6574)
      attachment protein (G)

<400> 429
Met Gly Ser Glu Leu Tyr Ile Ile Glu Gly Val Ser Ser Ser Glu Ile
 1               5                  10                  15
Val Leu Lys Gln Val Leu Arg Arg Ser Gln Lys Ile Leu Leu Gly Leu
                20                  25                  30
Val Leu Ser Ala Leu Gly Leu Thr Leu Thr Ser Thr Ile Val Ile Ser
        35                  40                  45
Ile Cys Ile Ser Val Glu Gln Val Lys Leu Arg Gln Cys Val Asp Thr
    50                  55                  60
Tyr Trp Ala Glu Asn Gly Ser Leu His Pro Gly Gln Ser Thr Glu Asn
65                  70                  75                  80
Thr Ser Thr Arg Gly Lys Thr Thr Thr Lys Asp Pro Arg Arg Leu Gln
                85                  90                  95
Ala Thr Gly Ala Gly Lys Phe Glu Ser Cys Gly Tyr Val Gln Val Val
```

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                100                     105                     110
Asp Gly Asp Met His Asp Arg Ser Tyr Ala Val Leu Gly Gly Val Asp
            115                     120                     125
Cys Leu Gly Leu Leu Ala Leu Cys Glu Ser Gly Pro Ile Cys Gln Gly
    130                     135                     140
Asp Thr Trp Ser Glu Asp Gly Asn Phe Cys Arg Cys Thr Phe Ser Ser
145                     150                     155                     160
His Gly Val Ser Cys Cys Lys Lys Pro Lys Ser Lys Ala Thr Thr Ala
                165                     170                     175
Gln Arg Asn Ser Lys Pro Ala Asn Ser Lys Ser Thr Pro Pro Val His
            180                     185                     190
Ser Asp Arg Ala Ser Lys Glu His Asn Pro Ser Gln Gly Glu Gln Pro
        195                     200                     205
Arg Arg Gly Pro Thr Ser Ser Lys Thr Thr Ile Ala Ser Thr Pro Ser
    210                     215                     220
Thr Glu Asp Thr Ala Lys Pro Thr Ile Ser Lys Pro Lys Leu Thr Ile
225                     230                     235                     240
Arg Pro Ser Gln Arg Gly Pro Ser Gly Ser Thr Lys Ala Ala Ser Ser
                245                     250                     255
Thr Pro Ser His Lys Thr Asn Thr Arg Gly Thr Ser Lys Thr Thr Asp
            260                     265                     270
Gln Arg Pro Arg Thr Gly Pro Thr Pro Glu Arg Pro Arg Gln Thr His
        275                     280                     285
Ser Thr Ala Thr Pro Pro Pro Thr Thr Pro Ile His Lys Gly Arg Ala
    290                     295                     300
Pro Thr Pro Lys Pro Thr Thr Asp Leu Lys Val Asn Pro Arg Glu Gly
305                     310                     315                     320
Ser Thr Ser Pro Thr Ala Ile Gln Lys Asn Pro Thr Thr Gln Ser Asn
                325                     330                     335
Leu Val Asp Cys Thr Leu Ser Asp Pro Asp Glu Pro Gln Arg Ile Cys
            340                     345                     350
Tyr Gln Val Gly Thr Tyr Asn Pro Ser Gln Ser Gly Thr Cys Asn Ile
        355                     360                     365
Glu Val Pro Lys Cys Ser Thr Tyr Gly His Ala Cys Met Ala Thr Leu
    370                     375                     380
Tyr Asp Thr Pro Phe Asn Cys Trp Arg Arg Thr Arg Arg Cys Ile Cys
385                     390                     395                     400
Asp Ser Gly Gly Glu Leu Ile Glu Trp Cys Cys Thr Ser Gln
                405                     410
```

<210> 430
<211> 46
<212> PRT
<213> human metapneumovirus

<220>
<223> Postulated HRA sequence of strain NL1/00

<400> 430

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Lys Thr Ile Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu
 1               5                  10                  15
Lys Lys Thr Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val
            20                  25                  30
Leu Ala Thr Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys
        35                  40                  45
```

<210> 431
<211> 46
<212> PRT
<213> human metapneumovirus

<220>

<223> Postulated HRA sequence of strain NL17/00

<400> 431
Lys Thr Ile Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu
1 5 10 15
Lys Thr Thr Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val
20 25 30
Leu Ala Thr Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys
35 40 45

<210> 432
<211> 46
<212> PRT
<213> human metapneumovirus

<220>
<223> Postulated HRA sequence of strain NL1/99

<400> 432
Lys Thr Ile Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu
1 5 10 15
Lys Gln Thr Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val
20 25 30
Leu Ala Thr Ala Val Arg Glu Leu Lys Glu Phe Val Ser Lys
35 40 45

<210> 433
<211> 46
<212> PRT
<213> human metapneumovirus

<220>
<223> Postulated HRA sequence of strain NL1/94

<400> 433
Lys Thr Ile Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu
1 5 10 15
Lys Thr Thr Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val
20 25 30
Leu Ala Thr Ala Val Arg Glu Leu Lys Glu Phe Val Ser Lys
35 40 45

<210> 434
<211> 29
<212> PRT
<213> human metapneumovirus

<220>
<223> Postulated HRB sequence of strain NL1/00

<400> 434
Asn Val Ala Leu Asp Gln Val Phe Glu Ser Ile Glu Asn Ser Gln Ala
1 5 10 15
Leu Val Asp Gln Ser Asn Arg Ile Leu Ser Ser Ala Glu
20 25

<210> 435
<211> 29
<212> PRT
<213> human metapneumovirus

<220>
<223> Postulated HRB sequence of strain NL17/00

<400> 435
Asn Val Ala Leu Asp Gln Val Phe Glu Asn Ile Glu Asn Ser Gln Ala
1   5   10   15
Leu Val Asp Gln Ser Asn Arg Ile Leu Ser Ser Ala Glu
            20   25

<210> 436
<211> 29
<212> PRT
<213> human metapneumovirus

<220>
<223> Postulated HRB sequence of strain NL1/99

<400> 436
Asn Val Ala Leu Asp Gln Val Phe Glu Ser Ile Glu Asn Ser Gln Ala
1   5   10   15
Leu Val Asp Gln Ser Asn Lys Ile Leu Asn Ser Ala Glu
            20   25

<210> 437
<211> 29
<212> PRT
<213> human metapneumovirus

<220>
<223> Postulated HRB sequence of strain NL1/94

<400> 437
Asn Val Ala Leu Asp Gln Val Phe Glu Ser Ile Glu Asn Ser Gln Ala
1   5   10   15
Leu Val Asp Gln Ser Asn Lys Ile Leu Asn Ser Ala Glu
            20   25

MICROORGANISMS

Optional Sheet in connection with the microorganism referred to on page 67-68, lines 1-30; 1-18 of the description [1]

A. IDENTIFICATION OF DEPOSIT [2]

Further deposits are identified on an additional sheet [3]

Name of depositary institution [4]

American Type Culture Collection

Address of depositary institution (including postal code and country) [4]

10801 University Blvd.
Manassas, VA 20110-2209
US

Date of deposit [5] January 19, 2001 Accession Number [6] I-2614

B. ADDITIONAL INDICATIONS [7] (leave blank if not applicable). This information is continued on a separate attached sheet

C. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE [8] (if the indications are not all designated States)

D. SEPARATE FURNISHING OF INDICATIONS [9] (leave blank if not applicable)

The indications listed below will be submitted to the International Bureau later [9] (Specify the general nature of the indications e.g., "Accession Number of Deposit")

E. ☐ This sheet was received with the International application when filed (to be checked by the receiving Office)

Mamie Holmes
(Authorized Officer)

☒ The date of receipt (from the applicant) by the International Bureau [10]

was 17 SEPTEMBER 2003

EKO
(Authorized Officer)

Form PCT/RO/134 (January 1981)